EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS -A RANDOMIZED CONTROLLED CLINICAL TRIAL

A Dissertation submitted in
Partial fulfillment of the requirements
for the degree of

MASTER OF DENTAL SURGERY

BRANCH – II
PERIODONTICS

THE TAMIL NADU DR. M.G.R. MEDICAL UNIVERSITY
Chennai – 600 032

2015 - 2018

CERTIFICATE BY THE GUIDE

This is to certify that **Dr.JENAPRIYA.R**, Post Graduate student (2015–2018) in the Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai – 600 003 has done this dissertation titled **"EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS – A RANDOMIZED CONTROLLED CLINICAL TRIAL"** under my direct guidance and supervision in partial fulfillment of the regulations laid down by **Tamil Nadu Dr. M.G.R. Medical University**, Chennai – 600 032 for **M.D.S.,** (Branch – II) **Periodontics** degree examination.

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DECLARATION BY THE CANDIDATE

I hereby declare that this dissertation titled **"EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS – A RANDOMIZED CONTROLLED CLINICAL TRIAL"** is a bonafide and genuine research work carried out by me under the guidance of **Dr.K MALATHI. M.D.S.,** HOD and Guide, Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai -600003.

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Last, but not the least, I thank **GOD ALMIGHTY** for his blessings.

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This agreement herein after the "Agreement" is entered into on this day ---------- between the Tamil Nadu Government Dental College and Hospital represented by its **Principal** having address at Tamil Nadu Government Dental College and Hospital, Chennai – 600 003, (hereafter referred to as, 'the college')

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Dr.JENAPRIYA .R, aged 27 years currently studying as **Post Graduate student** in Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai – 600 003, (hereafter referred to as 'the PG student and principal investigator')

And

Mrs. Dr .K MALATHI aged 46 years working as **HOD and Professor** in Department of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai

Whereas the PG student as part of his curriculum undertakes this research on **"EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS – A RANDOMIZED CONTROLLED CLINICAL TRIAL"** for which purpose the Co-investigators and the college shall provide the requisite infrastructure based on availability and also provide facility to the PG student as to the extent possible as a principal investigator.

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Sub: IEC review of the research proposals,

Title of the work:	Evaluation of locally delivered 1% metformin gel in the management of grade II furcation in chronic periodontitis- a randomized controlled clinical trial
Principal Investigator:	Dr.Jenapriya.R II year , MDS
Department :	Department of Periodontics Tamil Nadu Govt. Dental College & Hospital , Chennai-3

Thank you for submitting your research proposal , which was considered at the Institutional Ethics Committee meeting held on the 01.07 2016, at TN Govt. Dental College and the documents related to the study referred above were discussed and the modifications done as suggested and reported to us through your letter dated 29-07-2016 have been reviewed.

The decision of the members of the committee , the secretary and the Chairperson IEC of TN Govt. Dental College is here under:

Approved	Approved and advised to proceed with the study
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Revision	----------

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Chennai

CERTIFICATE OF 1% METFORMIN GEL PREPERATION

From

Prof ELANGO

Head of the Department ,

Department of Pharmaceutics ,

College of Pharmacy ,

Madras Medical College

TO

The Chairman,

Institutional Ethical Committee,

Tamil Nadu Government Dental College and Hospital,

Chennai.

Respected Sir,

Sub: Preparation of 1% Metformin gel

The Department of Pharmaceutics , College of Pharmacy, Madras Medical College, Chennai, has prepared and provided the 1% Metformin gel using Metformin hydrochloride powder, gellan gum, mannitol, sucralose , citric acid and methylparaben for fulfilling the needs of the thesis titled "Evaluation Of Locally Delivered 1% Metformin Gel In The Management Of Grade II Furcation In Chronic Periodontitis -A Randomized Controlled Clinical Trial " by Dr Jenapriya.R , IInd year P.G, Dept of Periodontics, Tamil Nadu Government Dental College and Hospital, Chennai.

Thanking You;

Yours sincerely,

23/02/17

(Prof ELANGO)

PROFESSOR AND HEAD

Place : 23/02/17

Date :

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ABSTRACT

Background:

Attaining periodontal regeneration is the ultimate aim of any sort of periodontal therapy. Bone regeneration is based on fundamental principles of bone biology and physiology. Metformin, a widely used antidiabetic drug has shown to have osteogenic potential. Hence in the present study, we explored the efficacy of locally delivered 1% Metformin gel in regeneration of bone in grade II furcation defect.

Aim: To evaluate the efficacy of locally delivered 1% Metformin gel in the management of grade II furcation in chronic periodontitis

Methods: A total of 20 patients with grade II furcation defect in chronic periodontitis were selected and divided into two groups of 10 each. The first group (study group) was treated with 1 % metformin gel and collagen membrane while the second group (control group) was treated by collagen membrane alone. Clinical parameters like gingival bleeding index(GBI), plaque index(PI), clinical attachment level (CAL), vertical probing depth, horizontal probing depth, were recorded at baseline ,3 ,6 and 9 months post operatively in both study and control group. Radiographically defect depth and defect fill was evaluated both in study and control group at an interval of 3, 6, 9 months. The radiographs were digitized using digital camera and images were analysed by Image J software.

Results: Significant reduction in postoperative mean vertical probing depth and horizontal probing depth was noticed in both the groups compared to baseline. Radiographically at the end of 9 months a significant defect fill was evident in study group than control group ($p=0.006$). Percentage of bone fill was greater in study group (73.70 ± 16.86) as compared to control group (56.10 ± 14.30) at 9 months.

Conclusion: A significant bone fill was noticed in furcation defects treated with 1% metformin and absorbable guided tissue regeneration membrane versus open flap debridement and absorbable guided tissue regeneration membrane without 1% metformin in chronic periodontitis.

Key words: Chronic periodontitis, metformin, guided tissue regeneration.

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LIST OF ABBREVIATIONS

MT	Metformin
CAL	Clinical Attachment Level
CEJ	Cemento–Enamel Junction
BMI	Basal metabolic rate
BOP	Bleeding on probing
GTR	Guided tissue regeneration
IOPA	Intra oral periapical radiograph
OPG	Orthopantamogram
PPD	Probing Pocket Depth
GBR	Guided bone regeneration
SD	Standard Deviation
SRP	Scaling and Root Planing
IBD	Intra bony defect
PRF	Platelet rich fibrin
OFD	Open flap debridement
GBI	Gingival bleeding index

BDX	Bovine-derived xenograft
PTFE	Polytetrafluoroethylene membrane
TMC	Trimethyline carbonate
HGF	Human gingival fibroblasts
HOB	Human osteoblast-like
MPM	Modified perforated bovine collagen membrane
BTP	Bio thermal plasma membrane
AMPK	Activated protien kinase
CM	Collagen membrane
FGM	functionally graded membrane
PDLF	Periodontal ligament fibroblast
ATV	Atrovastatin

INTRODUCTION

Diabetes mellitus is a pandemic metabolic disease affecting about 300 million of the world population [1]. Diabetes mellitus has been associated with formation of advanced glycation end products (AGEs) which ultimately lead to alveolar bone loss . A mainstay of pharmacological therapy for individuals with diabetes is the biguanide drug metformin. The exact mechanism of action of metformin has persistently remained elusive[2]. Along with life style modification, metformin drug therapy has improved HbA1c level, insulin sensitivity and secretion. It appears that metformin also has a therapeutic advantage in treatment of polycystic ovary syndrome (PCOS), gestational diabetes, kidney disease, heart disease and associated circulatory problems[3]. Metformin has been reported to effect bone turnover and alleviate fractures in diabetic patients ***(Vestergaard et al 2005)*** [4]. Metformin has shown to boost osteoblast proliferation and augment type 1 collagen formation [5].

Animal studies have proposed that metformin curtails receptor activator for nuclear factor-kappa B ligand (RANKL) and exhilarated osteoprotegerin expression in osteoblasts, there by restrain osteoclast differentiation and bone loss[5.] In a study on ligature-induced periodontitis, the metformin treatment has lead to a prompt diminution in alveolar bone loss[6]. Recently, ***Kanazawa*** and colleagues established osteogenic potential of metformin and proposed that metformin can induce the differentiation and mineralization of osteoblasts via activation of AMPK pathway and induction of endothelial nitric oxide synthase (eNOS) and bone morphogenetic protein-2 (BMP-2) expression[7]. Studies on local delivery of 1% metformin following phase 1 therapy and

treatment of intrabony defects in chronic periodontitis has delineated the osteogenic potential of metformin .[8,9]

Periodontitis is a chronic inflammatory disease ending in progressive loss of bone and supporting periodontal structures. Despite the fact that periodontally affected teeth respond well to larger part of therapy, morbidity is elicited with periodontally involved multi rooted teeth. Moderate to severe furcation defects management is a challenging quest for clinicians.

Clinical management of Class II furcation has baffled dentists over these years because of the difficulty in attaining desirable periodontal regeneration. Anatomical inaccessibility of furcation for oral hygiene maintenance as well open flap debridement procedure makes regeneration dubious.

Over the years periodontal osseous defects have been dealt by bone grafting .The use of autogenous grafts and allografts have been constrained due to risk of disease transmission and inadequate donor material. This propelled the development of alloplasts or synthetic bone substitutes for periodontal applications. Guided tissue regeneration (GTR) which is based on exclusion of epithelium from a periodontal defect, and thereby permitting selective repopulation of the defect with bone, cementum, and periodontal ligament, induce the desired regeneration. A physical barrier is placed over a periodontal defect to eliminate the undesired cells.

The purpose of the study is to evaluate the regeneration potential of 1% metformin gel with collagen membrane in treatment of class II furcation defects in molars.

AIM AND OBJECTIVES

AIM:

To evaluate the efficacy of locally delivered 1% Metformin gel in the management of grade II furcation in chronic periodontitis.

OBJECTIVES:

- To compare the clinical parameters - plaque index, gingival bleeding index, vertical probing depth, horizontal probing depth and clinical attachment before and after the treatment in the study group (group I).
- To compare the clinical parameters- plaque index, gingival bleeding index, vertical probing depth, horizontal probing depth and clinical attachment before and after the treatment in the control group (group II).
- To compare the clinical parameters - plaque index, gingival bleeding index, vertical probing depth, horizontal probing depth and clinical attachment before and after the treatment between the study and control group.
- Radiographic assessment of furcation defects before and after treatment with in study and control group.
- Radiographic assessment of furcation defects before and after treatment between study and control group.

REVIEW OF LITERATURE

GENERAL REVIEW

Periodontal disease is characterized by tissue inflammation and destruction of the tooth supporting structures that eventually leads to the loss of affected teeth.

The ultimate goal of periodontal therapy is not only to apprehend the progressive nature of periodontal disease, but also to recoup the supporting apparatus destroyed by the disease. During the last two decades, laborious efforts have been made to regenerate the lost periodontal tissue.

Terminologies: [10]

"Periodontal regeneration" is defined as the complete replacement of lost periodontal structure including formation of new cementum with inserting periodontal ligament fibers, bone and gingiva.

"New attachment" occurs, with the formation of new epithelium and new cementum with inserting new periodontal ligament fibers on a previously diseased root surface, where the periodontal ligament fibers were lost. New bone formation does not occur.

"Reattachment" is the term used to describe the reunion of root surface with preserved periodontal ligament tissue and the surrounding soft tissue.

"Periodontal repair" is the healing of wound after periodontal surgery with new tissue that does not replicate the structure and function of the destroyed tissue. There is formation of the junctional epithelium and gingival connective tissue

attachment at the same site of tissue injury, which is at a level more apical to bone destruction.

Furcation defects

Furcation involvement is defined as bone resorption and attachment loss in the interradicular space of multirooted teeth that results from plaque-associated periodontal disease. Such a condition will amplify the risk for tooth loss.

Therefore, furcation defects represent an ominous problem in the treatment of periodontal disease, in the view of the fact that furcation defect has got a complex and irregular anatomy. Moreover the presence of a broad radicular surface, which harbors more pathogenic microorganism compared to single rooted tooth make success of therapy cumbersome. Once the lesion has been established, the discrepancy in extent between the root surfaces and the periodontal soft tissues facing the bacterial insult may be responsible for a reduced healing response. Finally, the distal location in the arch and the difficult access may conceivably impair both self-performed and professional plaque control procedures in the furcation area, limiting their effectiveness[11].

Definition

Glossary of Periodontal Terms defines Furcation as "the area of a multi-rooted tooth where the roots diverge". It defines a furcation invasion as the "pathologic resorption of bone within a Furcation".[10]

Parts of Furcation

Furcation entrance: Transitional area between undivided and divided part of the root.

Furcation fornix: The roof of the furcation.

Degree of separation: The angle of separation between the roots.

Divergence: It is the distance between two roots which normally increases in apical direction.

The diagnosis of furcation involvement is made by clinical examination & careful probing with the specially designed probes (e.g., Naber's probe). Transgingival sounding may further define the anatomy of the furcation region [12].

Radiographic examination of the area is helpful, but lesions can be obscured by angulation of the beam and the radioopacity of neighboring structures.

Bjorn and Hjort 1982[13] assessed the radiographic prevalence, degree and development of bone destruction in mandibular molar furcations in a sample of 221 factory workers over a period of 13 years. The prevalence of furcation involvement steadily increased from an initial value of 18% to 32% at the end of the observation period. Third and second molars had higher frequencies of advanced destruction than first molars.

Ross & Thompson 1980[14] detected furcation involvement more frequently in maxillary molars by radiographic examination than clinical inspection, whereas the opposite was true for mandibular molars.

Glickman(1953)[15] was one of the first to classify furcation invasions based on the degree of lateral penetration of the periodontal destruction under the roof of the furcation. He divided them into the following four grades:

Grade-I: When there is soft-tissue lesion or pocket extending into the flute of the furcation, but the inter-radicular bone is intact. This involvement of the periodontium in the furcation area is without radiographic evidence of bone loss.

Grade-II: Loss of inter-radicular bone & pocket formation of varying depths into the furcation but not completely through the opposite side of the tooth. There is radiographic evidence of involvement.

Grade-III: Complete loss of inter-radicular bone with radiographic evidence presenting a small triangular radiolucency at the furcation area. There is a pocket formation that is completely probable to the opposite side of the tooth. However, the furcation is not visible clinically.

Grade-lV: Same features as those of Grade III except that loss of periodontal attachment & gingival recession has made the furcation clearly visible to a clinical examination.

Hamp et al 1975[16] described a classification which defined the horizontal extent of the furcation involvement.

Degree I / class 1: represents horizontal attachment loss of less than 3 mm within the furcation involvement.

Class-II: represents horizontal loss greater than 3 mm but not encompassing the total width of the furcation.

Class-III: denotes horizontal through and through destruction

The successful treatment of the furcation lesions depend on the degree of furcation involvement. Grade /class I lesion respond well to conservative approach like odontoplasty, root planing and minimal flap surgery. Grade / class III and IV lesions respond well to surgical therapy such as Widman flaps or tunnel preparations whereas Grade / class II furcation respond well to that of regenerative therapies by employing guided tissue regeneration. All these procedures will eventually aim at "NEW ATTATCHMENT"

GUIDED TISSUE REGENERATION

Focus on periodontal regenerative therapy started 3 decades back to find whether any part of the periodontium (periodontal ligament, cementum, alveolar bone or gingival connective tissue) possessed the capacity to regenerate the lost periodontal structure by formation of new attachment.

Melcher 1976[17] hypothesized certain cell populations residing in the periodontium have the potential to create new cementum, periodontal ligament,and alveolar bone provided they have the chance to repopulate the defect .These progenitor cells can be derived from

- ✓ Epithelial cells
- ✓ Cells from gingival connective tissue
- ✓ Cells from alveolar bone
- ✓ Cells from periodontal ligament

Nyman and Karring 1980 [18]study on beagle dogs to evaluate the regenerative capacity of extracted root placed in edentulous area of bone concluded that in addition to apical migration of junctional epithelium and regrowth of subgingival plaque, the type of cells which repopulate the wound area may jeopardize new connective tissue attachment.

Nyman, Gotlow , Karring **1982** [19] study on monkey concluded that the periodontal ligament cells possess the ability to reestablish connective tissue attachment.

Karring et al 1985[20] proposed that new attachment is formed by coronal migration of cells originating from the periodontal ligament.

Based on these landmark studies ***Nyman et al 1982*** introduced the concept of "*GUIDED TISSUE REGENERATION*" in which physical barrier is used to deflect the gingival connective tissue and the apically migrating oral epithelium away from the root surface and create a protected space over the defect that allows cells from the remaining periodontal ligament to selectively repopulate the root surface.

PERIODONTAL REGENERATION

The concept of selective cell repopulation aiming periodontal regeneration lead to the development of barrier membranes, commonly known as barriers or membranes for guided tissue regeneration.

Four stages are used to successfully regenerate bone and other tissues, abbreviated with the acronym PASS[21]

1 . Primary closure of the wound to promote undisturbed and uninterrupted healing.

2. Angiogenesis to provide necessary blood supply and undifferentiated mesenchymal cells.

3. Space creation and maintenance to facilitate space for bone in-growth.

4. Stability of the wound to induce blood clot formation and allow uneventful healing.

The first generation of guided tissue regeneration studies were carried out using nonresorbable expanded polytetrafluoroethylene membranes, which created the basis for the clinical use of this technique. Following this landmark study a variety of barrier membranes were introduced.

The design criteria for periodontal guided tissue regeneration devices include[22]

- Biocompatibility
- Cell exclusion
- Space maintenance
- Tissue integration
- Ease of use
- Biological activity

Minabe 1991[23] classified the membranes into two types.

1. Non resorbable membranes

2. Resorbable membranes

Based on further modifications that were being introduced, ***Gottlow 1993***[24]classified the membranes into three groups.

I First generation (Non-resorbable)

1. Millipore filter

2. Expanded polytetrafluoroethylene (ePTFE) membrane (Goretex)

3. Nucleopore membrane

4. Rubber dam.

II Second generation (Resorbable)

1. Collagen membrane

2. Polylactic acid membrane (Guidor)

3. Vicryl Mesh (Polyglactin 910)

4. Cargile membrane

5. Oxidised cellulose

6. Hydrolyzable polyester.

III Third generation (Resorbable with growth factors)

ABSORBABLE BARRIERS:

General considerations:

Absorbable barriers do not require additional surgery for removal, which reduces patient discomfort, chair-side time and related cost, while eliminating potential surgery related morbidity.

By their inherent nature, absorbable barriers offer limited control over the length of application. This is because the disintegration process starts upon placement in the tissues, and the ability of each individual to degrade a particular biomaterial may vary significantly, particularly for materials requiring enzymatic degradation (such as collagen) reviewing the biological rationale for guided tissue regeneration.

Minabe 1991[23] concluded that absorbable devices should maintain their in-vivo structure for at least four weeks. Others suggest longer time periods are necessary because of their biodegradability. Absorbable devices elicit inevitable and necessary tissue reactions that may influence wound healing.

Several complications such as early degradation, epithelial down growth along the material and premature loss of the material were reported following the use of certain materials.

Absorbable materials used for guided tissue regeneration devices fall in to two broad categories. Natural products and synthetic materials.

Natural products: Collagen has been used extensively for manufacture of biomedical devices because of its biologic and physical properties and ample availability.

Intrinsic collagen participates in soft tissue and bone healing. Exogenous collagen exhibits hemostatic activity, is able to attract and activate neutrophils and fibroblasts and interacts with various cells during tissue remodelling and wound healing[25]. These biological activities along with low immunogenicity make collagen an attractive biomaterial.Although collagen based devices have been in use since the early part of this century (gut suture), this biomaterial has experienced much wider use in the last two decades.

Collagen used for medical devices are derived from several animal sources including bovine skin, tendon, intestine or sheep–intestine. Isolation and purification follows one of the two ways. The first is enzymatic preparation of soluble collagen and the other is chemical extraction of fibrillar collagen from collagenous tissue. Following isolation and purification, collagen, is processed by several means to manufacture gels, sponges, filaments, membranes as reviewed by ***Khor Li.***[26]The most common processing is cross linking usually by glutraldehyde treatment.

A type I collagen guided tissue regeneration membrane approved for clinical use is manufactured from collagen derived from bovine deep flexor tendon (BioMend). This membrane is semi-occlusive and completely absorbed in four to eight weeks. The performance of the membrane appears to vary depending on the type of defect being treated. This variable performance may relate to a limited ability to support space provision and/or maintenance.

Another type I collagen membrane derived from calf pericardium and cross linked by diphenylphosphorylazide has been evaluated for guided tissue regeneration.

Pitaru et al 1989[27] studied the capacity of collagen membranes to prevent the apical migration of epithelium and to support new connective tissue attachment in experimental periodontal defects in dogs.

Tal et al 1992[28] performed a study which evaluated the ability of collagen membranes to act as biodegradable barriers that interfere with colonization of the root surface by gingival cells and allow selective repopulation of the denuded root surface by periodontal ligament-derived tissue. Over a 3-year period, experimental and control surgical procedures were performed on canine teeth in six beagle dogs and on premolars in three beagle dogs.

Results showed that the membranes partially prevented apical migration of epithelium during healing. Regeneration of new cementum, alveolar bone, and periodontal ligament like tissue was found in the studied premolars but notably absent on the canines.

Paul et al 1992[29] studied the use of collagen membrane to treat furcation defects. The results of this treatment were compared with the results of conventional therapy. For most clinical parameters, there was no statistically significant difference in the results of treatment with or without collagen membranes. Sites treated with a collagen barrier did exhibit statistically significant improvement in probing depth and horizontal osseous support; however, these findings cannot be attributed entirely to the placement of the collagen membrane.

Camelo et al 1998[30] made a clinical,radiographic and histologic evaluation of human periodontal defects treated with Bio-Oss® and Bio-Gide.

Four intrabony periodontal defects were treated: two received Bio-Oss alone and two were treated with a combination of Bio-Oss and Bio-Gide. Radiographs, clinical probing depths, and attachment levels were obtained pre-operatively and 6 to 9 months post-operative, and teeth and surrounding tissues were biopsied. Both treatments significantly improved clinical probing depths and attachment levels, and the radiographic appearance suggested osseous fill. Histologic evaluation revealed that both treatments produced new cementum with inserting collagen fibers and new bone formation on the surface of the graft particles. This regenerative effect was more pronounced using the BioOss/ BioGide combination, which resulted in 7mm of new cementum and periodontal ligament and extensive new bone incorporating the graft.

Tatakis et al. 1999[31] stated that when a collagen membrane is implanted in the human body it is resorbed by the enzymatic activity of macrophages and polymorphonuclear leucocytes.

Carmargo et al 2000[32] made a study to evaluate the clinical effectiveness of a bovine porous bone mineral used in combination with a porcine derived collagen membrane as a barrier in promoting periodontal regeneration in intrabony defects in humans. Experimental sites were grafted with bovine porous bone mineral and received a collagen membrane for guided tissue regeneration. Control sites were treated with an open flap debridement. Results: Pre-operative pocket depths, attachment levels and trans-operative bone measurements were similar for control and experimental sites. Surgical re-entry of the treated defects revealed a significantly greater amount of defect fill in favor of experimental sites. The results of this study indicate that clinical resolution of intrabony defects can be achieved using a combination of bovine porous bone mineral and an absorbable, porcine derived collagen membrane when employing a technique based on the principles of guided

tissue regeneration. The nature of the attachment between the newly regenerated tissue and the root surfaces need to be evaluated histologically to confirm the presence of new attachment.

Houser et al 2001[33]compared Bio-Oss (BO), an anorganic bovine bone xenograft, in combination with Bio-Gide (BG), a bio absorbable collagen barrier, to open-flap debridement (OFD) surgery in human mandibular Class II furcation defects. There was a statistically significant difference between BO/BG and OFD in all soft and hard tissue measurements with the exception of attachment level, recession, and alveolar crest resorption.

Nociti et al 2001[34] clinically evaluated an absorbable collagen membrane (Bio-Gide) and a non - absorbable polytetrafluoroethylene membrane (PTFE), associated with or without bone grafts, for the treatment of ligature-induced peri-implantitis defects in dogs. Experimental peri-implantitis was induced after abutment connection. Ligatures and abutments were removed after 1 month and the bone defects were randomly assigned to one of the following treatments: DB: debridement alone; GBR+BG-I: debridement plus PTFE membrane associated with mineralized bone graft (Bio-Oss); GBR+BG-II: debridement plus collagen membrane (Bio-Gide) associated with mineralized bone graft; GBR-I: debridement plus PTFE membrane; GBR-II: debridement plus collagen membrane; BG: debridement plus mineralized bone graft. The peri-implant bone defects were measured before and 5 months after treatment. Results showed the greatest percentage of vertical bone fill for GBR+BG-II (27.77+/-14.07) followed by GBR-II.

Sculean et al 2003[35]compared clinically the treatment of deep intrabony defects with a combination of a bovine-derived xenograft (BDX) and a bioresorbable

collagen membrane to access flap surgery. 1 year after surgery both therapies resulted in significant PD reductions and CAL gains, and treatment with BDX + collagen membrane resulted in significantly higher CAL gains than treatment with access flap surgery.

Strouvpolos et al 2004[36] made a comparative study of barrier membranes as graft protectors in the treatment of localized bone defects. Three saddle-type osseous defects were created bilaterally in edentulous areas of the mandible. The defects were filled with assayed, canine demineralized freezed-dried bone (DFDB) in a thermoplastic gelatin matrix. Using a randomized block design, four sites were covered with bio-gide. TMC membranes of four different porosities were used, one site was covered with a collagen membrane and one site consisted of DFDB alone (control). A total of 30 sites were reviewed microradiographically and underwent histomorphometric analysis for bone regeneration, soft tissue presence and remaining graft material. All sites exhibited uneventful healing. A significantly higher percentage of bone regeneration was seen in the sites protected by the PGA:TMC membrane (bio gide). The PGA: TMC membrane protected the DFDB-filled defect and allowed a greater amount of bone regeneration than the defect protected by the collagen membrane or the control.

Hartman GA et al 2004[37] evaluated the clinical and histologic aspects of anorganic bovine bone collagen with or without a collagen barrier. Six months post-surgery, clinical parameters were recorded prior to enbloc resection of teeth and adjacent grafted sites. The majority of sites showed a favorable clinical response with respect to probing depth reduction and clinical attachment gain. Histologic analysis demonstrated new bone, cementum, and periodontal ligament coronal to the reference notch in two of the eight specimens. Two sites demonstrated new attachment, and

four showed a long junctional epithelium. Periodontal regeneration is possible following a bone-replacement graft of Bio-Oss Collagen.

Kasaj et al 2008[38] evaluated the biological effects of various bio absorbable and non-resorbable membranes in cultures of primary human gingival fibroblasts (HGF), periodontal ligament fibroblasts (PDLF) and human osteoblast-like (HOB) cells invitro. Results from the present study suggested that GTR membrane materials, per se, may influence cell proliferation in the process of periodontal tissue/bone regeneration. Among the six membranes examined, the bioabsorbable membranes demonstrated to be more suitable to stimulate cellular proliferation compared to non resorbable PTFE membranes.

Urban et al 2011[39] evaluated the use of a new synthetic resorbable membrane with autogenous bone, either alone or in combination with anorganic bovine bone-derived mineral, for horizontal ridge augmentation and subsequent implant placement. Ridge measurements were obtained before and after augmentation, complications were recorded, and biopsy specimens were examined histologically. All implants have survived, with an average follow-up period of 45.88months (± 12.43 months). Histologic analysis of the selected augmentation sites showed new bone formation and good incorporation of the bovine bone mineral particles.

Bottino MC et al 2011[40] designed a periodontal membrane with a graded structure that allows tailoring of the layer properties to design a material system that will retain its physical, chemical and mechanical characteristics for a period long enough to optimize periodontal regeneration. The FGM consists of a core layer (CL) and two functional surface layers (SLs) interfacing with bone (nano-hydroxyapatite, n-HAp) and epithelial (metronidazole, MET) tissues. The CL comprises a neat

poly(dl-lactide-co-ε-caprolactone) (PLCL) layer surrounded by two composite layers composed of a protein/polymer ternary blend (PLCL:PLA:GEL). The CL structure demonstrated higher strength (8.7 MPa) and a more elastic behavior (strain at break 357%) compared with the FGM (3.5 MPa, 297%).

Ahamed .Y.Gamal et al 2013[41]compared traditional occlusive collagen membrane (OM) and modified perforated bovine collagen membrane (MPM). At 6- and 9-month observation periods, the MPM-treated sites showed a statistically significant improvement in PD reduction and CAL gain compared with the OM control group. Defect was significantly reduced with no significant difference between the two groups at 6- and 9-month observation periods. Crestal bone level was significantly higher in the MPM group when compared with that of the OM group at both observation periods. The postoperative differences between the two groups were 2 and 1.7 mm at 6 and 9 months, respectively, in favor of the MPM-treated sites.

Stoecklin-Wasmer et al 2013[42]published a systematic review on Guided tissue regeneration(GTR) with bioabsorbable collagen membranes (CM). Systematic review of randomized clinical trials were performed to assess the clinical efficacy of GTR procedures with CM, with or without bone substitutes, in periodontal infrabony defects compared with that of open flap debridement (OFD) alone. They concluded GTR with CM is beneficial for treatment of infrabony periodontal defects.

Yen C-C, Tu Y-K, Chen T-H, Lu H-K 2014 [43] published a systematic review and metaanalysis to find the value of extrapolating animal data on treatment of periodontal infrabony lesions, using GTR only or GTR + bone grafts, to human clinical results. Analysis indicated that animal models and human results showed

similar bone-filling ratios in infrabony defects treated with GTR only or with GTR + bone grafting.

Stamatoski et al 2017[44] did a comparative study on autologous PRF membrane and bio thermal plasma membrane (BTP) as GTR membrane. The BTP was found to be plasmin resistant and stable for 30 days in vitro and function as an excellent scaffold material for periosteal cells in vitro. In animal implantation study BTP was observed for at least 35days post implantation while control PRF was completely restored within 10days.

So-Hyoun Lee et al 2017[45]conducted a study to evaluate the efficacy of resorbable electron beam irradiated bacterial cellulose membranes (EI-BCMs) for guided bone regeneration (GBR). The electron beam irradiation (EI) was introduced to control the biodegradability of BC for dental applications. EI-BCMs had higher porosity than collagen membranes (CMs), and had similar wet tensile strengths to CMs. Micro-computed tomography (μCT) and histometric analysis in peri-implant dehiscence defects of beagle dogs showed that EI-BCMs has better properties. These results suggest that resorbable EI-BCMs can be used as an alternative biomaterial for bone tissue regeneration.

Arunjaroensuk S, et al 2017[46] compared stability of augmented bone between a synthetic resorbable membrane and a collagen resorbable membrane with guided bone regeneration (GBR) simultaneous with dental implant placement in 60 patients. Study revealed no statistically significant difference between the groups.

LOCAL DRUG DELIVERY

Ever since the introduction of systemic antibiotics, various drugs have been used in the treatment of periodontitis. The disadvantages of systemic antibiotics like bacterial resistance, superimposed infections, uncertain patient compliance, nausea, vomiting and gastrointestinal disturbances led to the introduction of local drug delivery as the treatment option[47].

Goodson et al 1979[48] assessed the feasibility of treating periodontal disease by controlled delivery of antibacterial agents from within periodontal pockets. Tetracycline-filled hollow fibers placed in the gingival sulcus were shown to have a dramatic effect both on the periodontal microflora and clinical manifestations of disease.

Classification

Various classification systems were evolved.

(I) Based on the application [Rams and Slots] 1996 [49]

1. Personally applied (in patient home self-care)

A. Nonsustained subgingival drug delivery

- Home oral irrigation
- Home oral irrigation jet tips
- Traditional jet tips
- Oral irrigation (water pick)
- Soft cone rubber tips (pick pocket)

B. Sustained subgingival drug delivery

2. Professionally applied (in dental office)

A. Nonsustained subgingival drug delivery Professional pocket irrigation

B. Sustained subgingival drug delivery

C .Controlled release devices

- ✓ Hollow fibers
- ✓ Dialysis tubing
- ✓ Strips
- ✓ Films

(II) Based on the duration of medicament release (*Greenstein and Tonetti 2000)*[50]

A. Sustained release devices – Designed to provide drug delivery for less than 24 hours.

B. Controlled release devices – Designed to provide drug release that at least exceeds 1 day or for at least 3 days following application ***(Kornman1993).***

(III) Depending on degradability.

1. Nondegradable devices (first generation)

2. Degradable devices (second generation)

Needleman & Watts[51] tested the adjunctive effect of 1% metronidazole gel irrigation into furcation areas with class II and III involvements during periodontal

maintenance with subgingival scaling. Clinically, no further improvement were seen for the furcations treated with metronidazole.

Nylund & Egelberg 1990[52] evaluated the therapeutic effects of subgingival irrigation with tetracycline as a supplement to mechanical debridement in furcations with class I, II and III involvements.

The professional irrigation of 50 mg/ml tetracycline solution was performed every second week for 3 months. One-year evaluation of attachment levels and pocket depths showed similar clinically negligible (1 mm) variation in both tetracycline and saline-irrigated furcations.

Minabe et al 1991[53]immobilized tetracycline in a cross-linked collagen film to obtain a slow, sustained release of the drug. The film has been subsequently used alone or in conjunction with root planing in furcation class II involvements in a controlled randomized clinical trial. A dramatic decrease in frequency of sites with bleeding on probing was noted in the group treated with a combination of tetracycline and mechanical debridement.

The magnitude of reduction was significantly greater than that produced by either root planing or tetracycline film alone throughout. Probing attachment levels and pocket depths were similarly reduced by the three treatment regimens.

Tonetti et al. 1998[54] showed that tetracycline-containing fibers exert a significant adjunctive pocket depth and bleeding reduction over that produced by scaling and root planing alone.

Rocha M.2001[55] studied the effect of alendronate on bone loss prevention in type 2 diabetes mellitus patients with periodontal disease and concluded that

alendronate induced more improvement in alveolar bone crest height than control therapy.

Deepak Prasad et al 2010[56]evaluated alendronate on the alveolar bone regeneration following mucoperiosteal flap surgery. Polymer impregnated gel based delivery of alendronate was performed in 15 chronic periodontitis patients of age 35-55years. Following surgical flap debridement, 0.1 ml alendronate gel and 0.1 ml placebo gel was placed at the experimental and control sites respectively. Clinical and radiographic parameters were recorded at baseline, three months and six months post-surgery. Alendronate was more effective in improving clinical and radiographic parameters compared to placebo.

A.R. Pradeep 2013 [57] used 1% alendronate gel as a local drug delivery system as an adjunct to scaling and root planing (SRP) for the treatment of 69 mandibular Class II furcation defects in comparison with placebo gel. Clinical parameters were recorded at baseline, 3 months, 6 months, and 12 months, and radiographic parameters were recorded at baseline, 6 months, and 12 months. Defect fill at baseline, 6 months, and 12 months was calculated on standardized radiographs using image analysis software. Following the study period an improved bone fill compared with placebo gel as an adjunct to SRP was recorded.

Pradeep .A.R 2010 [58] evaluated the effectiveness of 1.2mg Simvastatin controlled release gel as an adjunct to scaling and root planing in the treatment of chronic periodontits .At the end of 6months study intrabony defect fill was noticed in sites treated with simvastatin .

Chen S et al 2011 [59]investigated the effects of simvastatin/methylcellulose gel on bone regeneration in furcation defects in miniature pigs and observed

regeneration of alveolar bone in furcation defect sites, as it promotes the proliferation of osteoblasts.

Shrutigarg and A.R.Pradeep 2017[60]explored the efficacy of 1.2% rosuvastatin(RSV) and 1.2% atorvastatin (ATV) gels as a local drug delivery adjunct to scaling and root planing (SRP) for treatment of Class II furcation defects .Ninety patients with mandibular buccal Class II furcation defects were randomly allocated to three treatment groups: 1) SRP with placebo gel (group 1) ; 2) SRP with 1.2% RSV gel (group 2); and 3) SRP with 1.2% ATV gel (group 3). Clinical and radiographic parameters were recorded at baseline and after 6 months. Gels were redelivered at the respective sites at a 6-month recall appointment. All clinical and radiographic parameters were recorded again after 3 months (i.e., 9 months from baseline).They concluded that the RSV group showed significant improvement in all clinical parameters and significantly greater defect depth reduction compared with the ATV group in treatment of mandibular Class II furcation defects as an adjunct to SRP.

Vestergaard P et al 2005 [61] evaluated the relative fracture risk in patients with diabetes mellitus and concluded that the use of metformin drugs to control diabetes may reduce the association between diabetes and fractures.

Eun Jung Bak et al *2010* [62] did study on effect of metformin on ligature induced periodontitis around mandibular molars of rat .The effect of metformin on osteoblast, osteoclast, and adipocyte differentiation was assessed by the degree of mineralization, the formation of tartrate-resistant acid phosphatase–positive multinucleated cells, and the accumulation of triglycerides, respectively. Metformin augmented the mineralization two-fold. However, metformin was shown to exert no effects on osteoclast and adipocyte differentiation.

M.Silvina Molinuevo et al in 2010 [63] from his invivo and invitro study on bone marrow progenitor cells differentiation concluded that metformin causes osteoblastic differentiation of bone mesenchymal progenitor cells .

Mai QG et al 2011[64] from invivo and in vitro studies demonstrated that metformin reduces receptor activator of nuclear factor κB ligand (RANKL) and stimulates osteoprotegerin (OPG) expression in osteoblasts, further inhibits osteoclast differentiation and prevents bone loss in overectomized rats.

A.R.Pradeep et al 2015 [65] evaluated the efficacy of open-flap debridement (OFD) combined with PRF, 1% Metformin gel (MF) gel, and PRF + 1% MF gel in the treatment of intrabony defects (IBDs) in patients with chronic periodontitis . The PRF + 1% MF group showed greater improvements in clinical parameters, with greater percentage radiographic defect depth reduction compared to MF, PRF, or OFD alone in treatment of IBDs in patients with chronic periodontitis .

A.R.Pradeep et al 2013 [66] conducted the study to explore the efficacy of 0.5%, 1%, and 1.5% MF gel as a local drug delivery system in the treatment of intrabony defects following scaling and root planing .118 intrabony defects were treated with 0.5%, 1%, or 1.5% MF gel or placebo gel. Data was collected at baseline, 3 and 6 months. A significant increase in the pocket depth reduction, CAL gain, and improved IBD depth reduction compared to placebo in adjunct to SRP was noted. Study suggested that 1%metformin gel has more beneficial effects in treatment of intrabony defect.

Dr. Nishanth S. Rao, Dr. A R Pradeep 2013[67] conducted a study to compare the effect of 1% metformin gel as an adjunct to SRP in the management of vertical defects in smokers with generalized chronic periodontitis. A total of 50 patients were

randomly assigned as case group (SRP+1%MF) and control group where SRP alone was performed. Radiographs, clinical probing depth, attachment levels were obtained preoperatively and at 3rd and 6th month. At the end of 6 months more CAL gain with significant IBD fill at vertical defect sites treated with SRP plus locally delivered MF was found. This study demonstrates that 1% metformin gel have bone forming capacity in intra bony defects of smokers.

A.R. Pradeep et al 2015[68] performed a comparative study of open-flap debridement (OFD) combined with PRF, 1% MF gel, and PRF + 1% MF gel in the treatment of intrabony defects (IBDs).120 patients with single defect were categorized randomly to 4 treatment groups for the comparative study. Clinical and radiographic assessment was done at baseline and 9months postoperatively. PRF, 1% MF, and PRF + 1% MF groups showed significantly more PD reduction and CAL gain than the OFD-only group. The authors concluded that periodontal regeneration was more in PRF + 1% MF group compared to MF, PRF, or OFD alone in treatment of IBDs in patients with chronic periodontitis.

MATERIALS AND METHODS

The study population was selected from the Outpatient Section of the Department of Periodontics, Tamilnadu Government Dental College and Hospital, Chennai, India.

INCLUSION CRITERIA:

- Patients of age group between 35-50 years.

- Systemically healthy patients with clinical attachment level (CAL) ≥ 5mm ; bleeding on probing (BOP) and probing depth (PD) 5-6mm, furcation defect confirmed by periapical radiographs.

- Patients with no history of periodontal therapy in the past 6 months.

- Patients without any antibiotic treatment in last six months.

- Patients with established willingness and ability to perform adequate oral hygiene.

EXCLUSION CRITERIA:

- Systemic illness known to affect the outcomes of periodontal therapy such as diabetes mellitus, cardiac disease and immunocompromised conditions.

- Patients who have known allergy to metformin.

- Patients who are on systemic metformin.

- Alcoholics and smokers.

- Pregnant and lactating females were not included in the study.

Subjects:

A total of 20 patients with grade II furcation defect in chronic periodontitis were selected.

Study design:

The study is a randomized controlled clinical trial

Sex: Either sex

STUDY DESIGN: All the ethical principles were meticulously followed throughout the course of the study. Subjects for the study were selected randomly. After explaining the study procedure (**Annexures 1, 2**) written informed consent (**Annexures 3, 4**) was obtained from all the subjects selected for the study. Examination (**Annexures 5**) was preceded by a thorough medical and dental history of the subjects. Each subject underwent full-mouth periodontal probing and charting, and radiographic evaluation.

Sample size:

A total of 20 sites were selected randomly and divided into 2 groups.

Study group (group I): scaling and root planning followed by flap surgery with 1% metformin and collagen membrane in the furcation defect.

Control group (group II): scaling and root planning followed by flap surgery with collagen membrane in the furcation defect.

STUDY PROTOCOL:

1. Patients will be selected as per the inclusion & exclusion criteria.

2. Medical history and informed consent.

3. Complete periodontal examination using a mouth mirror, William's & Naber's periodontal probe under artificial light.

4. Intra-oral evaluation and periodontal examination using clinical periodontal parameters namely gingival bleeding index, Plaque index, Vertical and Horizontal pocket probing depth and Clinical attachment level.

5. Radiographic evaluation- OPG & IOPA.

6. Phase I therapy and re-evaluation of clinical parameters after 4-6 weeks.

7. Selection of study sites and random allocation into two groups.

8. Surgical procedure.

9. Post-operative care.

10. Clinical re-evaluation at the end of 3, 6 and 9 months.

11. Radiographic re-evaluation at the end of 3, 6 and 9 months

DRUG USED IN THE STUDY

Metformin ,a biguanide , has been widely used as antidiabetic agent for the treatment of type2 diabetes mellitus since the late 1950s .Metformin is one of the insulin sensitizing agents most commonly used for the management of different conditions associated with insulin resistance , such as type2 diabetes mellitus, metabolic syndrome and polycystic ovary syndrome. Nevertheless the precise

mechanism of action of metformin remains elusive. It is considered as insulin – sensitizing drug, lowering glycemic levels without increasing insulin secretion .Several sites of action have been proposed for metformin, including decreased hepatic glucose output, increased peripheral glucose uptake, and improved insulin secretion. It has also been shown that metformin may be helpful in the fight against heart disease, decreased sexual ability and circulation problems [69].

PREPARATION OF DRUG

Ingredients used:

- Metformin
- Gellan gum
- Mannitol
- Citric acid
- Sodium citrate
- Sucralose
- Methylparaben
- Propylparaben
- Water

PROCEDURE:

All the required ingredients were weighed accurately. Dry gellan gum powder was dispersed in 50ml of distilled water maintained at 95°C for 20 minutes using a magnetic stirrer (Remi magnetic stirrer 2MHLH , Mumbai, India) to facilitate hydration of gellan gum. The required amount of mannitol was added to the gellan gum solution with continuous stirring and the temperature was maintained above 80°C. Metformin was added with stirring. Finally, required amount of sodium citrate was dissolved in 10ml of distilled water and added to the mixture. The weight of the gel was monitored continuously during manufacturing and finally it was adjusted to 100gm with distilled water. The mixture containing gellan gum and metformin was allowed to cool to room temperature to form gel .[66]

CLINICAL ASSESSMENT:

The clinical parameters to be evaluated before and after phase I therapy and 9 months post surgically include,

SOFT TISSUE MEASUREMENTS:

1. Plaque index

2. Gingival bleeding index

3. Clinical attachment level (in - mm) (CAL)

4. Vertical probing depth

5. Horizontal probing depth at furcation level

Plaque Index [Silness and Loe 1964][70]

All teeth were examined at 4 sites each (disto-facial, facial, mesio-facial, lingual / palatal) and were scored as follows:

Criteria for Scoring:

Score 0: No plaque

Score 1: Plaque not visible to the naked eye, detected only by running the explorer or by using a disclosing agent.

Score 2: Thin to moderate accumulation of soft deposits within the gingival pocket or on tooth and gingival margin, visible to the naked eye.

Score 3: Abundance of soft matter within gingival pocket and/or on tooth surface and margin, inter-dental area stuffed with soft debris.

Calculation:

Plaque index per tooth = Total score / 4

$$\text{Plaque index per individual} = \frac{\text{Total P I per tooth}}{\text{Total number of teeth examined}}$$

Interpretation:

Score 0 - Excellent oral hygiene

0.1 to 0.9 - Good oral hygiene

1.0 to 1.9 - Fair oral hygiene

2.0 to 3.0 - Poor oral hygiene

Gingival Bleeding Index [Ainamo & Bay 1975][71]

Starting distobuccally, the probe was inserted slightly into the sulcus and run to the buccal and mesial surfaces of every tooth at an angle of about 45°. This was repeated for all teeth present. Probing was similarly carried out at palatal/lingual sites. Any gingival units that exhibited bleeding were recorded. The total number of bleeding sites per tooth was thus recorded for every tooth except the third molar.

Criteria for Scoring

Positive score (1) - Presence of bleeding within 10 seconds

Negative score (0) - Absence of bleeding

$$\% \text{ of bleeding sites} = \frac{\text{Total number of positive score} \times 100}{\text{Total number of surfaces of all teeth}}$$

Stent Preparation

Acrylic occlusal stents were fabricated over the study models. Self-cured acrylic was used for this purpose. The stent covered the occlusal and coronal 1/ 3rd of the labial and lingual surfaces of the teeth. It involved one tooth mesially and one distally to the study tooth. Vertical grooves were made to guide the placement of the probe in the same plane and direction repeatedly during measurements to avoid any variation. The recordings were made using a William's periodontal probe.

Vertical probing depth

A customized acrylic stent was prepared. An occluso apical groove in the stent was made using a tapering fissure bur to standardize the insertion of the probe. The stent was stored on the cast itself. The base of the stent served as the reference point (RP) to take the measurements. Vertical probing depth was calculated by measuring the distance from a fixed reference point on the stent to the base of the pocket (BP) along the groove using the William's periodontal probe and subtracting it by the distance from the fixed reference point to the gingival margin(GM).

Vertical probing depth = (RP ─ BP) ─ (RP─GM)

Horizontal probing depth was measured using a Naber's probe.

Clinical Attachment Level:

Clinical attachment level was calculated by measuring the distance from the reference point to the base of the pocket and subtracting by the distance from the reference point to the cemento-enamel junction (CEJ).

CAL= (RP ─ BOP) ─ (RP ─ CEJ)

RADIOGRAPHIC MEASUREMENTS:

- Intraoral periapical radiographs were taken for each site using long cone paralleling technique and XCP holders at baseline, 3 months, 6 months and 9 months postoperatively and evaluated. The radiographs were digitized using digital camera and images were analyzed by Image J software. The following anatomical landmarks of the intrabony defect were identified on the radiograph images based on criteria set by ***Bjorn et al***[72] and by ***Schei et al*** [73]

1. CEJ: The cemento-enamel junction of the tooth with the intrabony defect

2. AC: The most coronal position of the alveolar bone crest of the intrabony defect when it touches the root surface of the adjacent tooth before treatment, the top of the crest.

3. BD : The most apical extension of the intrabony destruction where the periodontal ligament space still retained its normal width before treatment, the bottom of the defect.

If restorations were present, the apical margin of the restoration was used to replace the CEJ as a fixed reference point.

The following linear measurements were performed [74]

1. CEJ to bottom of the defect (CEJ to BD)

2. CEJ to furcation fornix (CEJ to FX)

Depth of the furcation defect at baseline = (CEJ to BD) - (CEJ to FX)

Correction factor: In order to estimate distortion between the consequent radiographs, an anatomically non-variable distance i.e. the root length (distance from the CEJ to the root apex (CEJ to RA)) was measured on all the radiographs. The correction factor (CF) was calculated as follows:

$$\frac{\text{CEJ to RA (baseline)}}{\text{CEJ to RA (post-op)}} = \text{Correction Factor}$$

In this study the measurement between cemento enamel junction and furcation fornix is taken for calculation of correction factor.

4. Defect fill (DF) = FX to BD (baseline) - [FX to BD (post op) x CF]

5. Defect fill percentage (DF %) = [defect fill/defect depth (baseline)] x 100

SURGICAL PROCEDURE:

- Extra oral antisepsis and intra oral antisepsis were performed with 5% povidone iodine solution and 0.2% Chlorhexidine digluconate rinse respectively. The operative site was anaesthetized with 2% Lignocaine HCl with adrenaline (1:80,000) using block and infiltration techniques.

- Crevicular incisions were made on the facial and lingual surfaces, extending one tooth on each side of the defect tooth using the Bard Parker blade No.15. A full thickness muco periosteal flap was reflected using the periosteal elevator. After reflection of the flap and exposure of furcation defect, a thorough surgical debridement of soft and hard tissue was done using the area specific Gracey curette. Debridement was followed by copious 0.9% normal saline irrigation.

- In case group (group I) ,following open flap debridement, furcation was filled with 1% metformin gel using a blunt cannula tip and was slightly overfilled . GTR membrane was trimmed according to the size of area being treated and adapted to the defect area .

- In control group (group II), open flap debridement was done. Furcation defect was debrided. GTR membrane was trimmed according to the size of area being treated and adapted to the defect area.

- The muco periosteal flaps were repositioned and secured using 3-0 braided black silk sutures. Periodontal dressing (Coe-pacTM) was placed.

- All patients were prescribed systemic antibiotics (Amoxycillin 500mg thrice daily, Metronidazole 400mg twice daily) and analgesics (Ibuprofen 400 mg thrice daily) for 1 week.

ARMAMENTARIUM:

For clinical examination

- Mouth mirror
- UNC 15 probe
- Naber's probe
- Kidney tray
- Cotton rolls
- Sterilized disposable gloves, head cap, facemask
- IOPA film
- Radiographic grid
- Customized acrylic stent

For Phase I Therapy

- Mouth mirror
- UNC 15 probe

- Kidney tray
- Naber's probe
- Ultrasonic scaler (Guilin Woodpecker,UDS-J ultrasonic scaler)
- Cotton rolls
- Sterilized disposable gloves, head cap, facemask
- Disposable syringes
- Local anesthetic solution
- Gracey Curettes

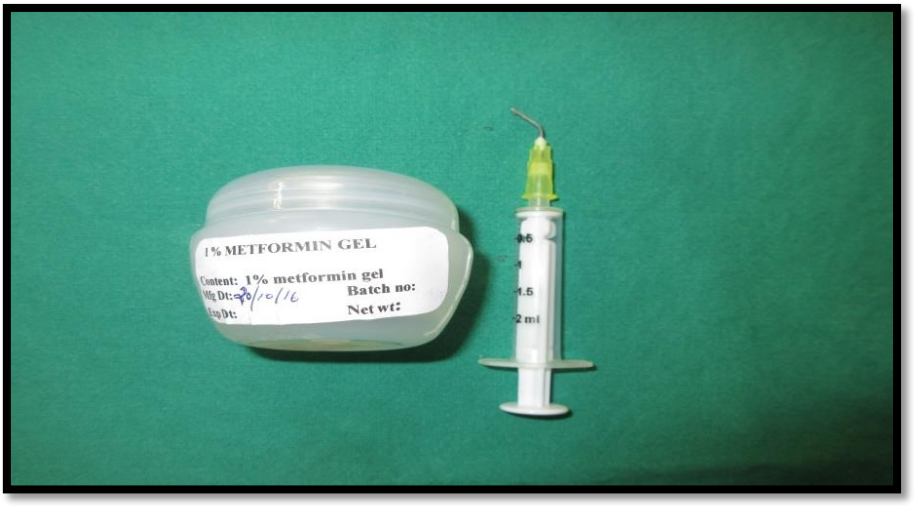
For surgical procedure :

- Mouth mirror
- Naber's probe
- UNC15 probe
- Dental tweezers
- Surgical gloves
- Disposable mask
- Local anesthesia
- Bard Parker blade no 15 and straight and contra-angled B.P handle .

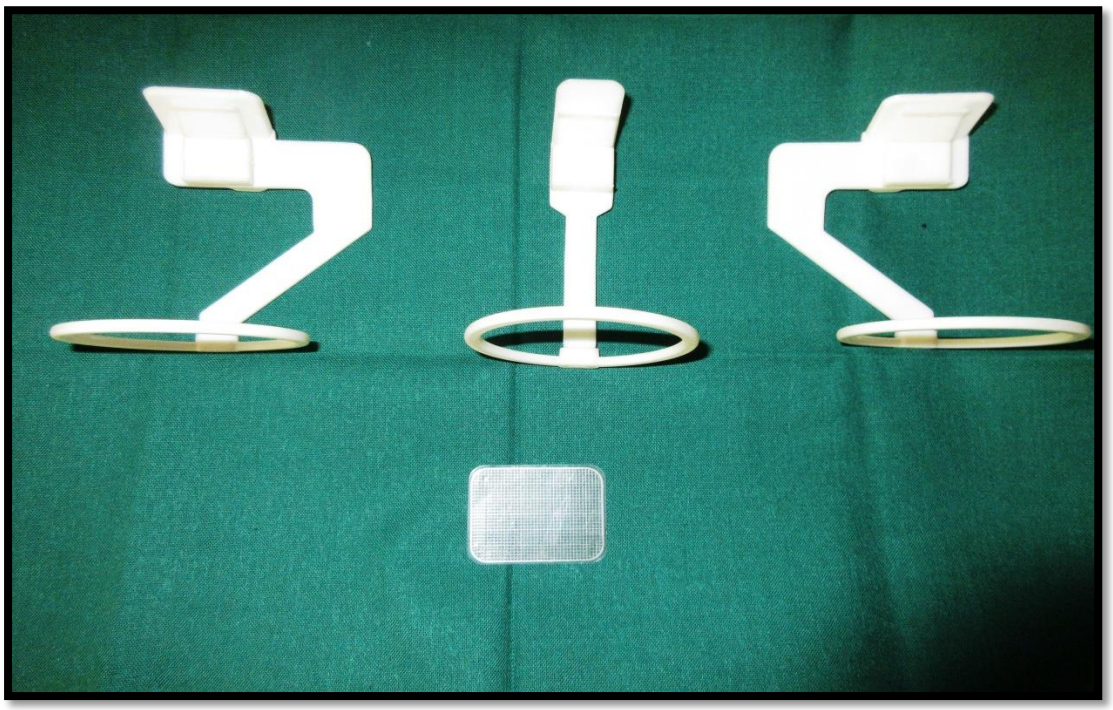
- Periosteal elevator
- Gracey curettes and universal curette (Columbia 4R-4L)
- Straight and Curved scissors
- Saline irrigation syringe
- Dappen dish
- 1% Metformin gel
- Blunt cannula
- GTR membrane (PerioCol)
- Suture material 3-0 braided black silk
- Needle holder
- Cement spatula and Glass slab
- Periodontal dressing (Coe-pacTM)

Photograph 1: Surgical Armamentarium

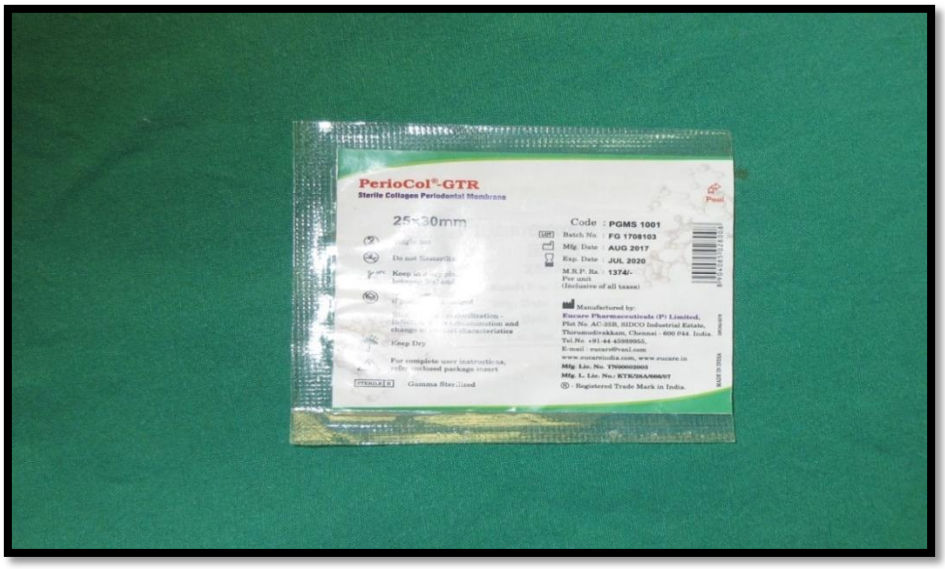
Photograph 2: 1% Metformin gel and delivery unit



Photograph 3: XCP Holders and Radiographic Film Grid

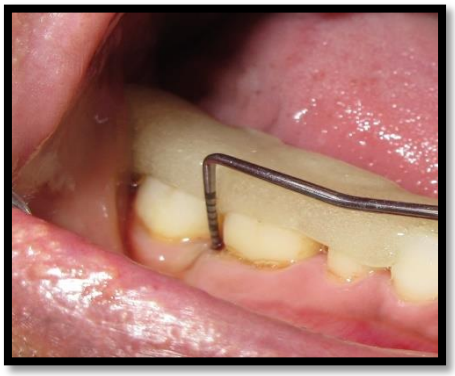


Photograph 4: PerioCol GTR Membrane



PHOTOGRAPH 5 : GROUP I (STUDY GROUP) INTRA ORAL PHOTOGRAPHS

Photograph 5(a): Measurement of vertical probing depth



Photograph 5(b): Grade II molar furcation

Photograph 5 (c): 1% metformin gel delivery to furcation

Photograph 5 (d): Adaptation of collagen membrane

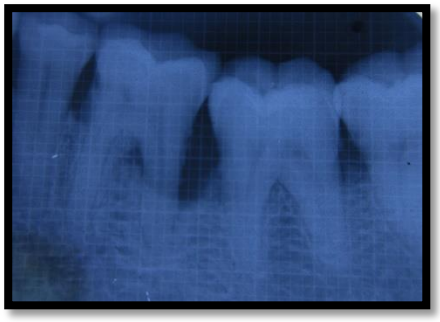
Photograph 5 (e): 9 months post-operative

Vertical Probing depth

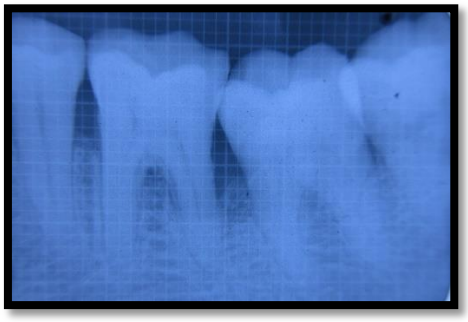
Horizontal Probing depth

PHOTOGRAPH 6: GROUP I- RADIOGRAPHIC VIEWS

Photograph 6(a): Baseline

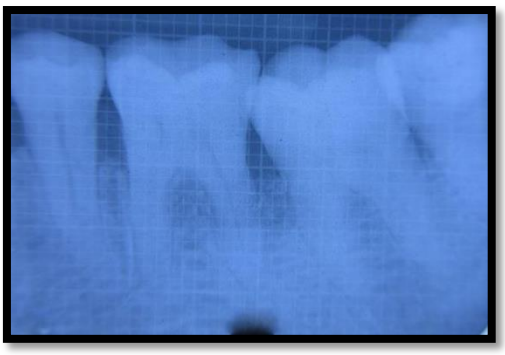


Photograph 6 (b): At 3 months



Photograph 6 (c): At 6 months

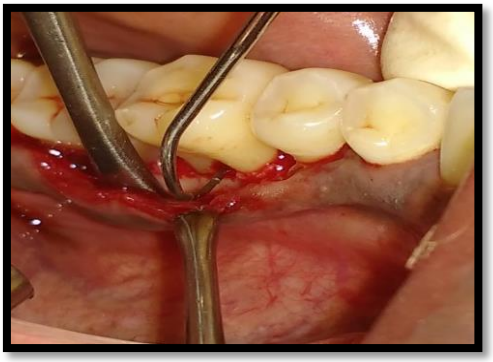
Photograph 6 (d): At 9 months



PHOTOGRAPH 7: GROUP II (CONTROL GROUP) INTRA ORAL PHOTOGRAPHS

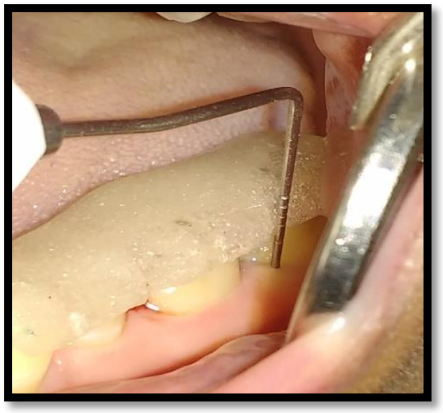
Photograph 7 (a): Measurement of vertical probing depth

Photograph 7 (b): Grade II molar furcation



Photograph 7 (c): Adaptation of collagen membrane

Photograph 7 (d): 9 months post-operative

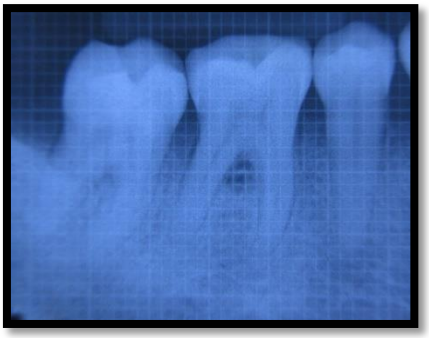


Vertical Probing depth

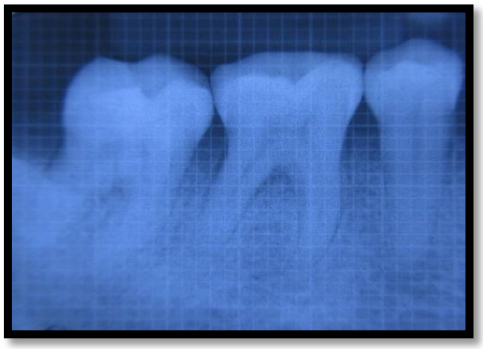
Horizontal Probing depth

PHOTOGRAPH 8 : GROUP II- RADIOGRAPHIC VIEWS

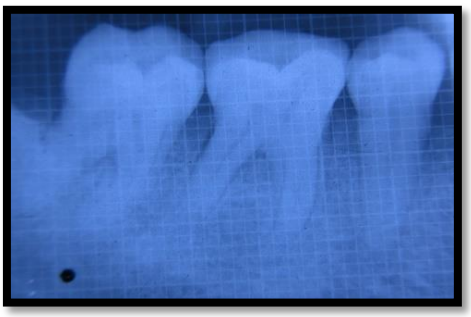
Photograph 8 (a): Baseline



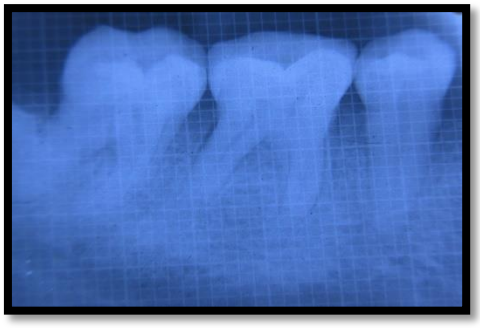
Photograph 8 (b): At 3 months



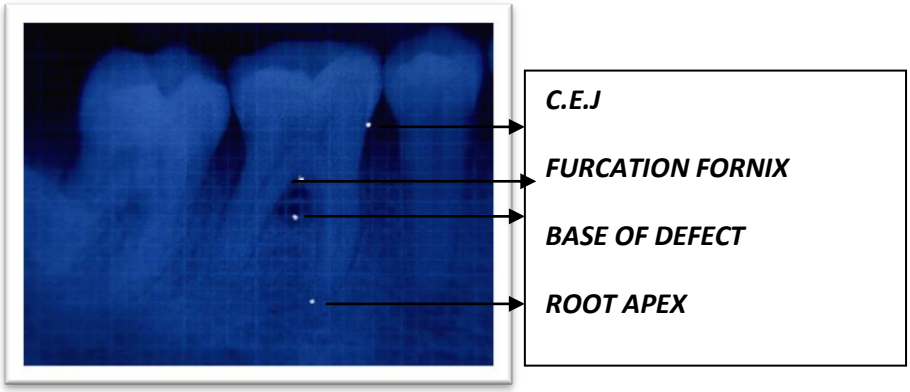
Photograph 8 (c): At 6 months



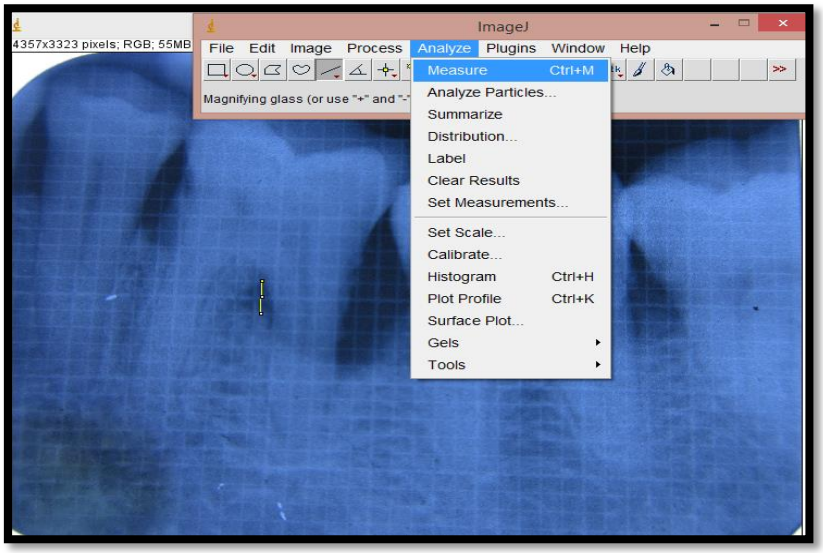
Photograph 8 (d): At 9 months



Photograph 9: Radiographic Landmarks



Photograph 10: Radiographic image analysis by Image J software



STATISTICAL ANALYSIS

The statistical analysis was done using the computer software program SPSS version 16 (Statistical Package for Social Science, Version 16). Descriptive data are presented as mean ± SD and range values.

Data of parameters vertical and horizontal probing pocket depth(VPD and HPD mm) 9 months, clinical attachment level CAL (mm) baseline, plaque index (PI) 9 months for inter group I and group II were found to be non – parametric using Shapiro-Wilk normality test, hence Mann Whitney U test was applied. Data of parameters plaque index (PI) Baseline, vertical pocket depth VPD mm -9 months in group II, clinical attachment level(CAL) 9 months for inter group I and group II was found to be parametric using Shapiro-Wilk normality test, hence paired sample t test was applied. Fisher Exact Test was done for intra group analysis of Gingival Bleeding Index (GBI) scores at baseline and at 9 months.

Repeated measures Anova test was used for intragroup comparison of radiological parameters defect depth (DD) and paired t test for defect fill(DF),and defect fill percentage(DF%). Independent sample t test was used for intergroup comparison of all radiographic parameters.

p value

The **p value** or calculated probability was the estimated probability of rejecting the null hypothesis (H0) of a study question when that hypothesis was true. The smaller the p-value, the more significant the result was said to be. All P-values are two tailed, and confidence intervals were calculated at the 95% level. Differences between the two populations were considered significant when $p \leq 0.05$.

STATISTICAL FORMULAE USED FOR DATA ANALYSIS

Independent sample t test formula:

$$t = \frac{\bar{X}_1 - \bar{X}_2}{\sqrt{\left(\frac{(N_1 - 1)s_1^2 + (N_2 - 1)s_2^2}{N_1 + N_2 - 2}\right)\left(\frac{1}{N_1} + \frac{1}{N_2}\right)}}$$

Paired sample t test formula

$$t = \frac{\Sigma d}{\sqrt{\frac{n\left(\Sigma d^2\right) - \left(\Sigma d\right)^2}{n-1}}}$$

Mann Whitney U Test:

$$U_1 = n_1 n_2 + \frac{n_1(n_1 + 1)}{2} - R_1$$

$$U_2 = n_1 n_2 + \frac{n_2(n_2 + 1)}{2} - R_2$$

Fisher Exact Test formula:

$$p = \frac{\binom{A+C}{A}\binom{B+D}{B}}{\binom{N}{A+B}} = \frac{(A+B)!(C+D)!(A+C)!(B+D)!}{A!\,B!\,C!\,D!\,N!}$$

Repeated measures ANOVA

$$\mathrm{SS}_{\text{total}} = \sum_{i-1}^{a}\sum_{j-1}^{n_i}\sum_{k-1}^{t} Y_{ijk}^2 - Nt\overline{y}_{...}^2$$

$$\mathrm{SS}_{\text{treat}} = t\sum_{i-1}^{a} n_i \overline{y}_{i..}^2 - Nt\overline{y}_{...}^2$$

$$\mathrm{SS}_{\text{error(a)}} = t\sum_{i-1}^{a}\sum_{j-1}^{n_i} \overline{y}_{ij.}^2 - t\sum_{i-1}^{a} n_i \overline{y}_{i..}^2$$

$$\mathrm{SS}_{\text{time}} = N\sum_{k-1}^{t} \overline{y}_{..k}^2 - Nt\overline{y}_{...}^2$$

$$\mathrm{SS}_{\text{treat x time}} = \sum_{i-1}^{a}\sum_{k-1}^{t} n_i \overline{y}_{i\cdot k}^2 - Nt\overline{y}_{...}^2 - \mathrm{SS}_{\text{treat}} - \mathrm{SS}_{\text{time}}$$

RESULT

Analysis of clinical parameters:

Plaque index:

Intragroup analysis:

Group I: The mean plaque index score of group I at baseline was 1.75± 0.8 (Mean ± SD) and the mean plaque index at 9 months was 0.33±0.10. The mean reduction was 1.425 which was found to be significant (p=0.002).

Group II: The mean plaque index score at baseline was 1.60±0.8 and at 9 months was 0.29±0.15. The mean reduction was 1.370 which was found to be significant statistically (p=0.002).

Intergroup analysis:

The mean difference between plaque index at 9 months was statistically not significant (p= 0.56).

Gingival Bleeding Index

Intragroup comparison

Group I: The mean GBI score at baseline was 82.69±3.3 and mean GBI at 9 months was 17.4±5.5. The mean reduction was 60.450 which was statistically significant (p=0.00).

Group II: The mean GBI score at baseline was 81.2±2.5 and mean GBI at 9 months was 20.72±2.36. The mean reduction was 65.29 which was statistically significant (p=0.00).

Intergroup comparison:

GBI intergroup at baseline cannot be compared as there is no difference between group I and group II GBI at 9 months, no statistical significance was seen (p=0.09) using fisher exact test.

Vertical Probing pocket depth

Intragroup comparison

Group I: The mean vertical pocket depth at baseline was 6.20±1.03 and at 9 months was 2.80±.42. The mean reduction in pocket depth from baseline to 9 months was 3.50 which was statistically significant (p=0.000).

Group II: The mean pocket depth at baseline was 6.10±1.1 and at 6 months was 2.4±0.5. The mean reduction in pocket depth from baseline to 9 months was 3.7 which was statistically significant (p=0.000).

Intergroup comparison The mean difference in pocket depth between group I and group II at baseline was 0.10 and at 9 months was 0.40 which were statistically not significant (p=0.84, p=0.07 respectively).

Horizontal Probing pocket depth

Intragroup comparison

Group I: The mean horizontal pocket depth at baseline was 6.1± 0.9 and at 9 months was 1.60±0.69. The mean reduction in pocket depth from baseline to 9 months was 4.50 which was statistically significant (p=0.000).

Group II: The mean pocket depth at baseline was 5.10±0.87 and at 9 months was 1.80±0.420. The mean reduction in pocket depth from baseline to 9 months was 3.30 which was statistically significant (p=0.000).

Intergroup comparison

The mean difference in pocket depth between group I and group II at baseline was 0.40 and at 9 months was 0.20 which were statistically not significant (p=0.2, p=0.44 respectively).

Clinical Attachment level

Intragroup comparison

Group I: The mean attachment level at baseline was 6.5 ±0.97 and at 9 months was 3.00 ± 0.66. The mean gain in attachment level from baseline to 9 months was 3.5 which was statistically significant (p=0.00).

Group II: The mean attachment level at baseline was 6.6 ± 0.96 and at 9 months was 2.6± 0.51. The mean gain in attachment level from baseline to 9 months was 4 which was statistically significant (p=0.00).

Intergroup comparison

Mean difference in attachment level between group I and group II at baseline was 0.1 and at 9months was 0.40 which were statistically not significant (p=0.82, p=0.152 respectively).

RADIOGRAPHIC PARAMETERS

1. Defect depth

Intragroup comparison

Baseline comparison analysis revealed no significant differences between defects for group I and group II furcations.

Group I : The mean defect depth at baseline was 3.03± 0.61, at 3 months was 1.83 ± 0.64 , at 6 months was 1.28 ± 0.80 and at 9 months was 0.74 ±0.66

The mean difference in defect depth from baseline to 3 months was 1.21 which was statistically significant (p = 0.000) .The mean difference in defect depth from baseline to 6 months was 1.75 which was also statistically significant (P=0.001). The mean difference in defect depth from baseline to 9 months was 2.29 which was also statistically significant (P=0.001).

The mean difference in defect depth from 3 months to 6 months was 0.55 which was statistically significant (p=0.017). The mean difference in defect depth from 3 months to 9 months was 1.084 which was statistically significant (p=0.00).

The mean difference in defect depth from 6 months to 9 months was 0.532 which was statistically significant (p=0.004).

Group II :

The mean defect depth at baseline was 2.67 ± 0.52, at 3 months was 2.06 ± 0.57, at 6 months was 1.56 ± 0.42 and at 9 months was 1.14 ±0.38.

The mean difference in defect depth from baseline to 3 months was 0.60 which was statistically significant (p = 0.001) .The mean difference in defect depth from baseline

to 6 months was 1.108 which was also statistically significant (p=0.000). The mean difference in defect depth from baseline to 9 months was 1.527 which was also statistically significant (p=0.000)

The mean difference in defect depth from 3 months to 6 months was 0.507 which was statistically significant (p=0.001). The mean difference in defect depth from 3 months to 9 months was 0.926 which was statistically significant (p=0.010). The mean difference in defect depth from 6 months to 9 months was 0.419 which was statistically not significant (P=0.072).

Intergroup comparison

At 3 months mean difference in defect depth between group I and group II was 0.24 which was statistically not significant (p=0.40).

At 6 months mean difference in defect depth between group I and group II was 0.28 which was statistically not significant (p=0.35).

At 9 months mean difference in defect depth between group I and group II was 0.39 which was statistically not significant (p=0.125).

Defect Fill

Intragroup comparison

Group I: The mean defect fill at 3 months was 1.20 ± 0.51 , at 6 months was 1.84 ± 0.55 and at 9 months was 2.2 ± 0.53.

The mean difference in defect fill from 3 months to 6 months was 0.64 which was statistically significant (p = 0.020). The mean difference in defect fill from 3 months to 9 months was 1.084. which was statistically significant (p = 0.000).The mean

difference in defect fill from 6 months to 9 months was 0.44 which was statistically significant (p = 0.049).

Group II : The mean defect fill at 3 months was 0.60 ± 0.31, at 6 months was a 1.108 ± 0.35 and at 9 months was 1.52±0.56

The mean difference in defect fill from 3 months to 6 months was 0.507 which was statistically significant (p = 0.002). The mean difference in defect fill from 3 months to 9 months was 0.926 which was statistically significant (p = 0.005). The mean difference in defect fill from 6 months to 9 months was 0.419 which was statistically significant (p = 0.036)

Intergroup comparison

At 3 months mean difference in defect between group I and group II was 0.604 which was statistically significant (p=0.005).

At 6 months mean difference in defect between group I and group II was 0.736 which was statistically significant (p=0.002).

At 9 months mean difference in defect between group I and group II was 0.763 which was statistically significant (p=0.006).

Defect Fill %

Intragroup comparison

Group I: The mean defect fill percentage at 3 months was 39.20 ± 16.16 ,at 6 months was 58.80 ± 18.09 and at 9 months was 73.70±16.86 .

The mean difference in defect fill from 3 months to 6 months was 19.6 which was statistically significant (p = 0.017). The mean difference in defect fill from 3 months

to 9 months was 34.5 which was statistically significant (p = 0.001). The mean difference in defect fill from 6 months to 9 months was 14.9 which was statistically significant (p = 0.005).

Group II :

The mean defect fill percentage at 3 months was 22.4 ± 12.16, at 6 months was a 39.10±11.23 and at 9 months was 56.10±14.30.

The mean difference in defect fill percentage from 3 months to 6 months was 16.70 which was statistically significant (p= 0.016). The mean difference in defect fill percentage from 3 months to 9 months was 33.70 which was statistically significant (p = 0.002). The mean difference in defect fill percentage from 6 months to 9 months was 17.00 which was statistically significant (p = 0.024).

Intergroup comparison

At 3 months mean difference in defect fill percentage between group I and group II was 16.80 which was statistically significant (p=0.017).

At 6 months mean difference in defect fill percentage between group I and group II was 19.70 which was statistically significant (p=0.009).

At 9 months mean difference in defect fill percentage between group I and group II was 17.60 which was statistically significant (p=0.022).

Group I

S.NO	AGE (YEARS)	SEX (M/F)	PI (BASELINE)	GBI(%) (BASELINE)	VPD(mm) (BASELINE)	HPD(mm) (BASELINE)	CAL(mm) (BASELINE)	PI 9MONTHS	GBI(%) 9MONTHS	VPD(mm) 9MONTHS	HPD(mm) 9MONTHS	CAL(mm) 9months
1	34	F	1.8	86.4	7	6	7	0.5	28.2	3	2	3
2	37	M	2.4	84.2	5	5	6	0.5	21.2	3	1	3
3	43	F	0.75	76.8	6	6	6	0.25	24.5	2	1	2
4	38	F	0.75	83.7	6	6	7	0.25	15.3	2	1	3
5	35	M	2.8	85.2	5	5	7	0.4	17.3	3	2	3
6	41	F	2.6	83.6	7	7	5	0.35	14.2	3	3	4
7	36	M	2.5	79.2	5	5	5	0.35	12.3	3	1	3
8	43	M	0.75	78.3	8	8	8	0.2	11.2	3	2	2
9	41	M	1.0	83.2	6	6	7	0.25	13.4	3	2	4
10	38	F	2.2	86.3	7	7	7	0.25	16.4	3	1	3

Group II

S.NO	AGE (YEARS)	SEX (M/F)	PI (BASELINE)	GBI(%) (BASELINE)	VPD(mm) (BASELINE)	HPD(mm) (BASELINE)	CAL (mm) (BASELINE)	PI 9MONTHS	GBI(%) 9MONTHS	VPD(mm) 9MONTHS	HPD(mm) 9MONTHS	CAL(mm) 9MONTHS
1	41	F	2.4	83.4	6	6	7	0.2	21.2	3	2	3
2	45	F	2.3	79.4	6	6	6	0.2	24.2	2	2	3
3	38	M	1	78.3	5	5	7	0.25	18.3	3	2	3
4	39	F	0.25	82.5	5	4	6	0.20	19.4	2	2	3
5	43	M	2.5	84.9	6	4	6	0.7	21.5	2	1	3
6	47	M	1.6	83.4	7	6	7	0.3	21.6	2	2	3
7	37	F	1.9	82.1	5	5	5	0.2	24.6	3	1	3
8	45	M	2.3	78.4	8	5	8	0.20	20.1	2	2	2
9	51	F	0.50	77.5	8	4	8	0.4	19.4	3	2	3
10	48	M	1.9	82.1	5	6	6	0.4	17.3	3	2	4

TABLE 1: CLINICAL PARAMETERS

TABLE 2: RADIOGRAPHIC MEASUREMENTS

GROUP I

	BASELINE			AFTER 3MONTHS				AFTER 6 MONTHS				AFTER 9 MONTHS			
S.NO	CEJ-BD	CEJ-BD	DD-BL	CEJ-BD 3	CEJ-FX 3	DD	CF3	CEJ-BD6	CEJ-FX6	DD-6	CF6	CEJ-BD9	CEJ-FX9	DD9	CF9
1	5.53	2.86	2.67	4.04	3.04	1	0.94	4.06	3.12	0.94	0.92	4.1	3.86	0.24	0.74
2	6.16	3.47	2.69	4.55	3.09	1.46	1.12	4.05	2.98	1.07	1.16	3.84	3.04	0.8	1.14
3	7.12	3.3	3.82	5.91	3.2	2.71	1.03	5.35	3.15	2.2	1.05	4.58	3.15	1.43	1.04
4	6.91	3.43	3.48	5.8	3.52	2.28	0.97	5.06	3.1	1.96	1.11	4.26	3.43	0.83	1
5	6.55	3.56	2.99	5.64	3.09	2.05	1.15	4.64	3.82	0.82	0.93	3.68	3.48	0.2	1.02
6	6.37	3.42	2.95	4.48	3.35	1.13	1.02	3.96	3.11	0.85	1.1	3.58	3.4	0.18	1
7	5.91	3.82	2.09	5.2	3.6	1.6	1.06	4.17	3.6	0.57	1.06	4.13	3.87	0.26	0.99
8	5.63	3.26	2.37	4.88	3.04	1.84	1.07	4.07	3.12	0.95	1.04	4	3.11	0.89	1.04
9	7.55	4.13	3.42	5.68	4.31	1.37	0.96	4.08	3.57	0.51	1.16	3.98	3.58	0.4	1.15
10	6.89	2.98	3.91	6.01	3.12	2.89	0.96	5.85	2.91	2.94	1.02	5.1	2.84	2.26	1.04

GROUPII

	BASELINE			AFTER 3 MONTHS				AFTER 6MONTHS				AFTER 9MONTHS			
S.NO	CEJ-BD	CEJ-FX	DD-BL	CEJ-BD3	CEJ-FX	DD3	CF3	CEJ-BD6	CEJ-FX6	DD-6	CF6	CEJ-BD9	CEJ-FX9	DD9	CF9
1	6.15	3.92	2.23	5.19	3.41	1.78	1.15	5.26	4.17	1.09	0.94	5.1	4.2	0.9	0.93
2	6.33	3.89	2.44	6.1	3.95	2.15	0.98	5.96	4.31	1.65	0.9	5.11	4.31	0.8	0.9
3	6.98	3.86	3.12	5.53	3.68	1.85	1.05	5.35	3.75	1.6	1.03	5.2	3.74	1.46	1.03
4	6.57	3.76	2.81	6.37	4.11	2.26	0.91	6.2	4.14	2.06	0.91	5.9	4.12	1.78	0.91
5	5.84	3.58	2.26	4.89	3.36	1.53	1.07	5.13	3.96	1.17	0.9	4.89	3.34	1.55	1.07
6	7.62	3.81	3.81	6.57	3.32	3.25	1.15	5.93	3.9	2.03	0.98	4.93	3.9	1	0.97
7	5.87	3.78	2.09	5.08	3.88	1.2	0.97	4.75	3.67	1.08	1.03	4.13	3.21	0.92	1.17
8	6.89	4.22	2.67	6.04	4.08	1.96	1.03	5.63	4.36	1.27	0.97	5.02	4.21	0.81	1
9	6.48	3.53	2.95	6.11	3.42	2.69	1.03	5.86	3.62	2.24	0.98	5.11	3.61	1.5	0.97
10	5.46	3.15	2.31	5.02	3.01	2.01	1.05	4.89	3.47	1.42	0.91	4.08	3.38	0.7	0.93

TABLE 3 : RADIOGRAPHIC PARAMETERS

CASE							
S.NO	DD-BL	DD-3	DD-6	DF-9	DF%3	DF%6	DF%9
1	.67	1.67	1.73	2.43	62	65	72
2	2.69	1.23	1.62	1.89	45	56	57
3	3.82	1.11	1.62	2.39	29	42	72
4	3.48	1.2	1.52	2.65	34	43	71
5	2.99	0.94	2.17	2.79	31	72	93
6	2.95	1.82	2.1	2.77	61	71	93
7	2.09	0.49	2.38	1.83	23	71	87
8	2.37	0.53	1.42	1.48	22	59	62
9	3.42	2.05	2.91	3.02	59	85	88
10	3.91	1.02	0.97	1.65	26	24	42
CONTROL							
S.NO	DD -BL	DD-3	DD-6	DD-9	DF%3	DF%6	DF%9
1	2.23	0.45	1.14	1.33	20	51	59
2	2.44	0.29	0.79	1.64	11	32	67
3	3.12	1.27	1.52	1.66	40	48	53
4	2.81	0.55	0.75	1.03	19	26	36
5	2.26	0.73	1.09	0.71	32	48	31
6	3.81	0.56	1.78	2.81	14	46	73
7	2.09	0.89	1.01	1.17	42	26	55
8	2.67	0.71	1.4	1.86	26	52	69
9	2.95	0.26	0.71	1.45	8	24	49
10	2.31	0.3	0.89	1.61	12	38	69

TABLE 4 : COMPARISON OF CLINICAL PARAMETERS- GROUP I AND GROUP II

	CASE			CONTROL			Group I V/s Group II			
	At baseline Mean ±SD	At 9months Mean ±SD	P value	At baseline Mean ±SD	At 9months Mean ±SD	P value	At baseline Mean diff	P value	At 9monts Mean diff	P value
PI	1.75 ± 0.8	0.33 ± 0.10	0.010*	1.6±.0.8	0.29±0.15	0.007*	0.090	0.812	0.035	0.569
VPD	6.2±1.03	2.8±0.42	0.00*	6.1±1.1	2.4±0.51	0.00*	0.10	0.84	0.40	0.074
HPD	6.1±0.9	1.6±0.69	0.00*	5.1±0.8	1.8±0.42	0.00*	1.00	0.2	-0.2	0.49
CAL	6.5±0.97	3.0±0.66	0.00*	6.6±0.96	2.6±0.51	O.OO*	0.1	0.8	0.4	0.15
GBI	82.69 ± 3.3	17.4 ± 5.5	0.00*	81.2± 2.5	20.72 ±2.36	0.00*	1.49	0.283	-3.35	0.096

Wilcoxon sign rank test & paired sample T test for intragroup comparisons ***Significant**

Mann –Whitney U test for intergroup comparison

TABLE 5: COMPARISON OF RADIOGRAPHIC PARAMETERS – GROUP I AND GROUP II

	Group I					Group II					Group I v/s Group II					
	At baseline	At 3 months	At 6 months	At 9 months		At baseline	At 3 months	At 6 months	At 9 months		At 3months		At 6 months		At 9 months	
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	P value	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	P value	Mean diff	P value	Mean diff	P value	Mean diff	P value
Defect depth	3.03±0.6	1.8±0.6	1.2±0.8	0.7±0.6	0.00*	2.6±0.5	2.06±0.5	1.5±0.42	1.14±0.38	0.00*	-0.23	0.40	-0.28	0.34	-0.39	0.24
Defect fill	-	1.20±0.5	1.7±0.52	2.2±0.5	0.00*	-	0.6±0.31	1.1±0.3	1.52±0.6	0.00*	0.605	0.00*	0.736	0.00*	0.763	0.00*
Defect Fill %	-	39.2±16	58.8±18	73±16	0.00*	-	22.4±12	39±11.2	56±14	0.00*	16.8	0.01*	19.7	0.00*	17.6	0.2

Repeated measures Anova for intra group comparison

Independent sample T test for intergroup comparison

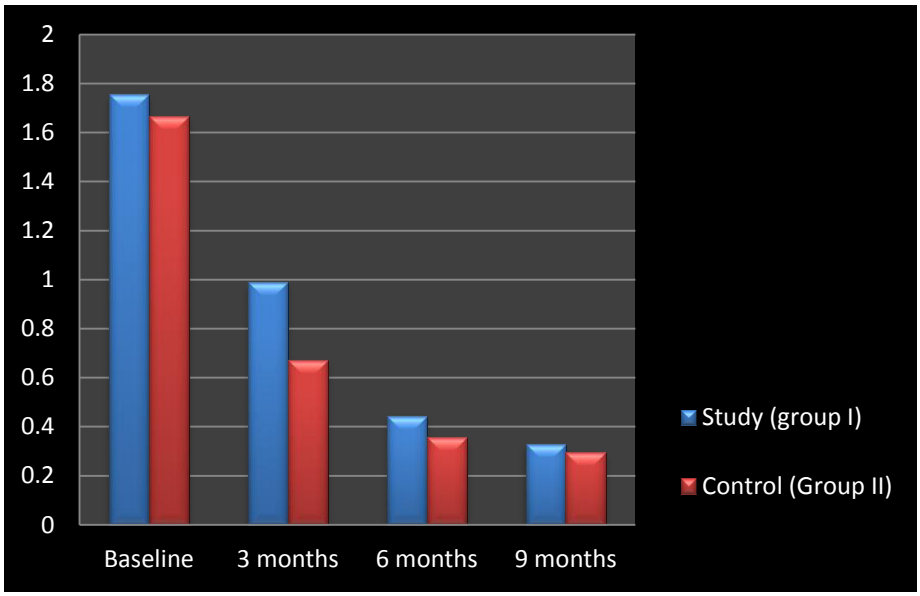


Figure 1: Comparison Of Plaque Index (PI) between study (Group I) and control group (Group II).

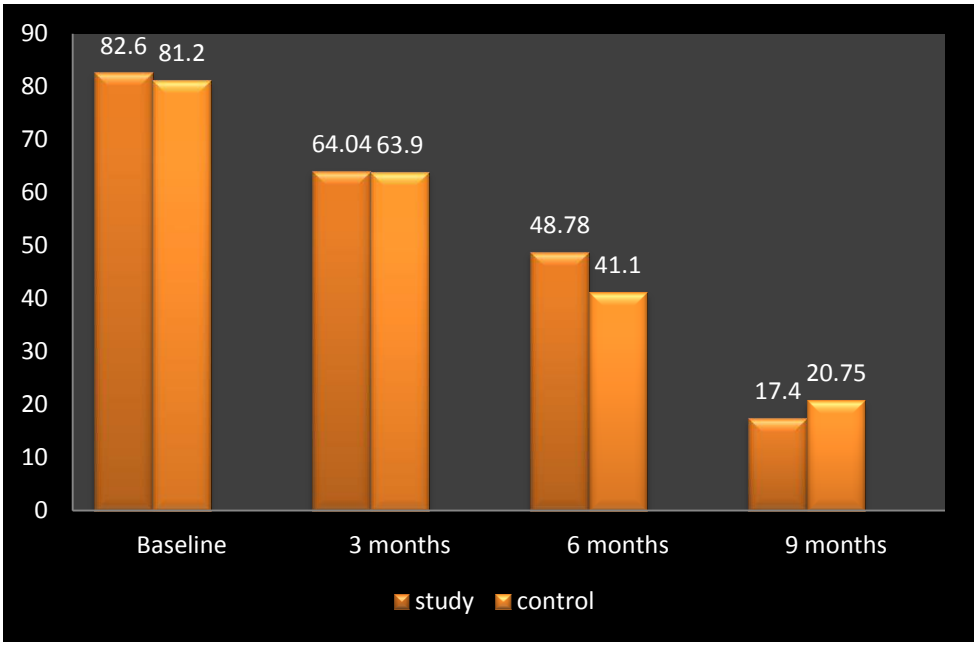


Figure 2 : Comparison of Gingival Bleeding Index between study and control group

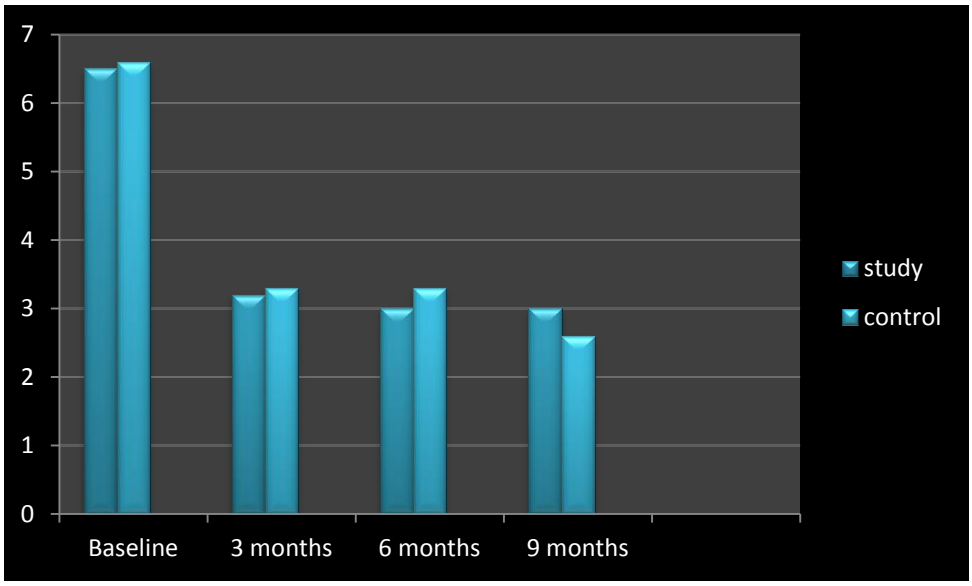


Figure 3: Comparison of CAL in study(Group I) and control group (Group II)

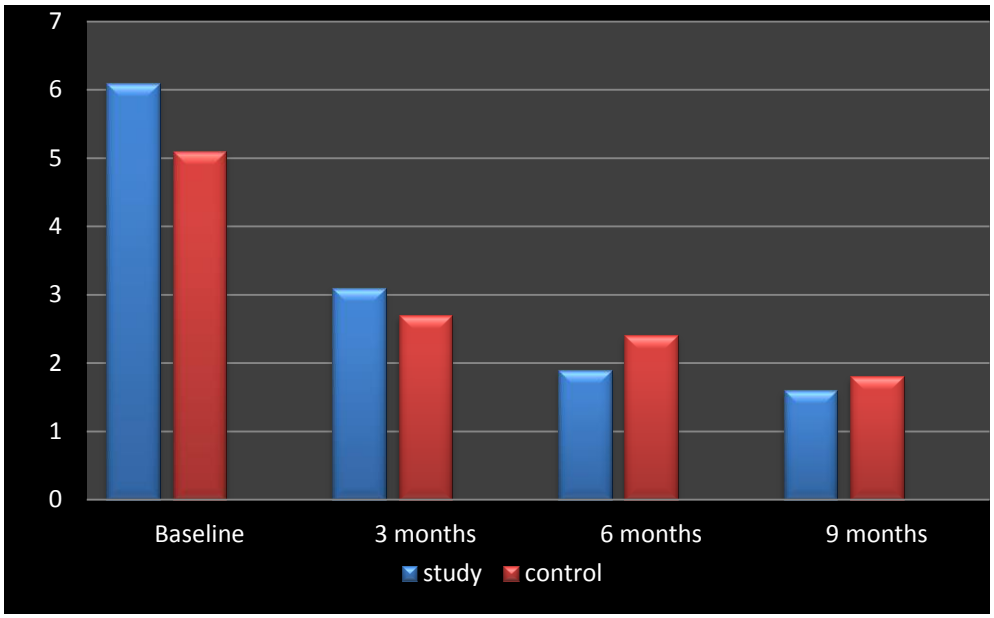


Figure 4 : Comparison of Horizontal probing depth (HPD) in study (Group I) and control group(Group II).

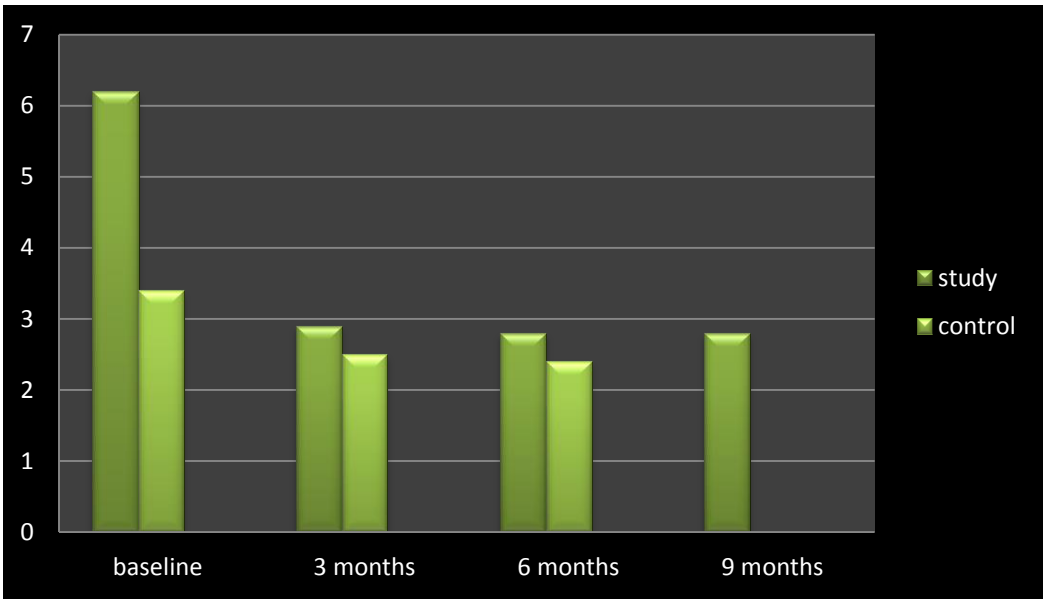


Figure 5: Comparison of Pocket Probing Depth (PPD) in study and control group

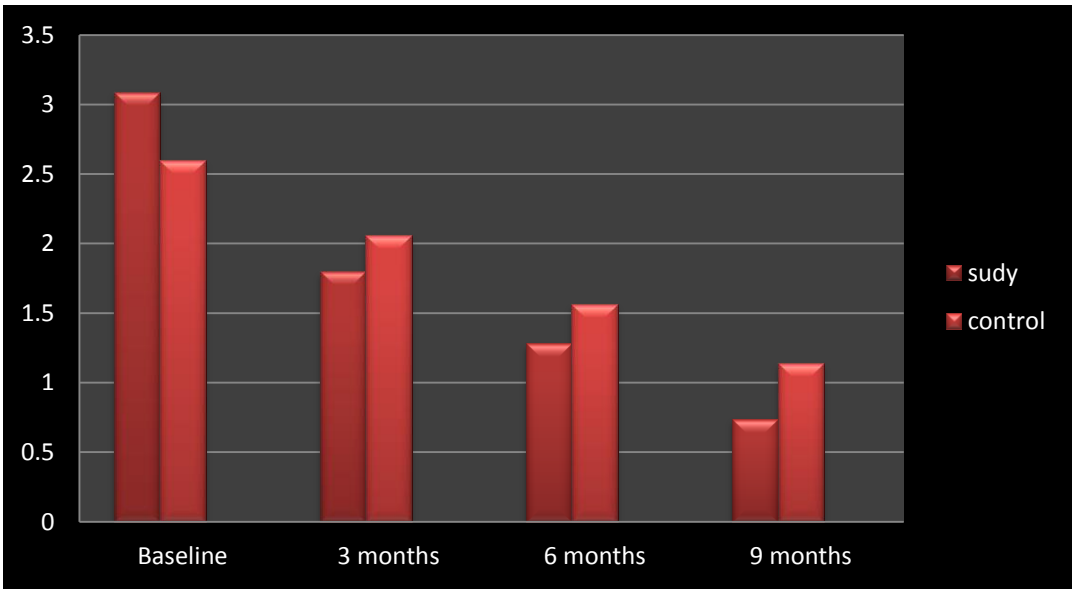


Figure 6: Comparison of defect dimension (DD) in study and control group

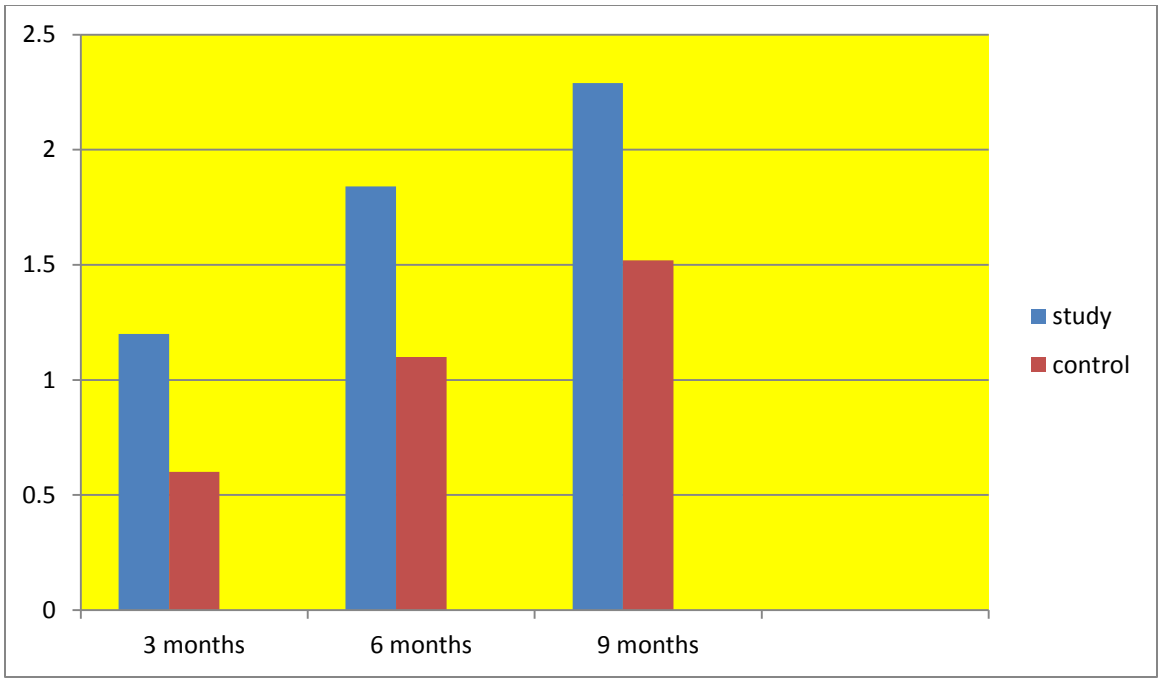


Figure 7: Comparison of defect fill between study and control group

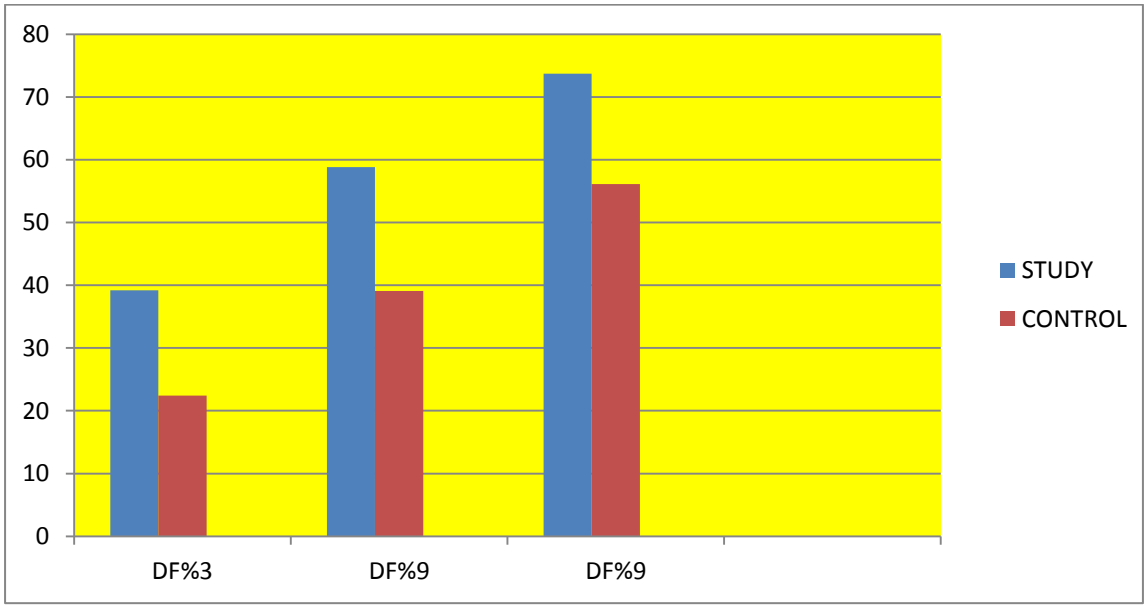


Figure 8: Comparison of defect fill % between study and control group

DISCUSSION

Attaining "regeneration"- the ultimate zenith of any sort of periodontal therapy, in a furcation defect is quite confronting to most of the clinicians. The complex surgical anatomy and hardship in instrumentation are the two main root elements hindering the road to regeneration.[75] Despite the fact that predictable closure of furcation defect through periodontal regeneration is still not a reality in clinical practice , combination of guided tissue regeneration therapy with an expedient graft material have proved to bring forth better results .

The current study evaluates the efficacy of 1% metformin gel with bio absorbable collagen membrane in the management of furcation defects.

Metformin, a biguanide family of drug ,is quite familiar among diabectologist worldwide for its blood sugar lowering effect in type 2 diabetes patients.[76] In addition to its efficacy in lowering blood glucose levels, metformin has the clinical advantage of inducing mild weight reduction in people with high BMI with a minimal risk of hypoglycemia.[77]

Metformin improves insulin sensitivity and secretion and decreases insulin resistance. In addition to Type II diabetes mellitus and associated cardiovascular complications, metformin is also considered as a therapeutic option for other diseases associated with insulin resistance, such as polycystic ovary syndrome (PCOS) and gestational diabetes.[78]

In vitro and in vivo studies in animal models have demonstrated antiproliferative action suggesting that metformin can be used as anticancer drug.[79]

Vestergaard et al ´s study on diabetic patients taking metformin, paved a path for promoting metformin as a bone regenerating factor[61].

The ability of metformin to persuade the differentiation and mineralization of osteoblasts through AMPK pathway activation and induction of endothelial nitric oxide synthase (eNOS) was demonstrated invitro by ***Kanazawa etal 2008.***[80]

Metformin causes a direct increase in bone marrow progenitor cells followed by osteoblastic maturation and trigger ALP activity and type 1 collagen synthesis.[81]

Metformin has shown to elevate the expression of insulin like growth factor and Runx2 which promote osteogenesis [82]

A.R Pradeep etal 2013 reported that 1% metformin concentration brought superior results in inducing bone formation than any other concentration.[66]

Side effects of metformin when systemically taken like diarrhea, muscle pain , weakness ,numbness, and stomach pain is not elicited following a local drug delivery. On the other hand local drug delivery of metformin upgrades the concentration of the drug at the desired site thereby eliminating the need of multiple applications.

Guided tissue regeneration embarked to a new era of less invasive clinical practice with resorbable collagen membrane. The resorbable membranes markedly demolished the risk of microbial invasion and loss of regenerated attachment; furthermore it enhanced the tissue coverage and curtailed barrier exposure.

Collagen is the most abundant protein of human body which forms the main frame work of the periodontium. Collagen has numerous biological properties which

are desirable such as having low immunogenicity, attracting and activating gingival fibroblast cells and being haemostatic[83]

In the current study a total of 20 patients from age group 35-50 of both sex were selected with chronic periodontitis and grade II furcation involvement and were assigned randomly into study (Group I) and control (Group II)groups . After compilation of phase I therapy, the sites were reexamined after 4 weeks, and surgical intervention by open flap debridement was planned. The study group furcation defects were treated with 1% metformin gel and collagen membrane was adapted over the filled defect. In the control group, furcation defects were debrided meticulously and collagen membrane alone was adapted.

Comparison of clinical parameters – plaque index, gingival bleeding index, vertical probing depth , horizontal probing depth and clinical attachment levels were done at 3, 6 and 9 months. Radiographic evaluation of defect depth , defect fill and defect fill % was done in the same time interval of 3,6 and 9months .

In this study all patients except one responded favorably with treatment procedures. Barrier membrane exposure was found in one patient and 1mm gingival recession was noticed in 3 patients.

In this study a reduction in plaque index and gingival bleeding index was observed in both study and control group at 9 months post operatively. The mean reduction in plaque index score was statistically significant post surgically both in control and study group. The mean difference between the two groups was not statistically significant post surgically for the same . The mean reduction in gingival bleeding index was also statistically significant at 9 months both in case and control group. Between the groups, there was no difference in the gingival bleeding index

score. These results are similar to the study done by ***A.R.Pradeep etal 2013***[67] in which the plaque index scores between two groups were not significant statistically.

The mean reduction in the vertical probing depth and horizontal probing depth was highly statistically significant in both study and control groups at 9 months post operatively compared to the baseline values. The mean reduction in pocket depth from baseline to 9 months post surgically was not statistically significant on comparing the study and control group. These findings were similar to the study by ***Lekovic et al (1989)*** who compared open flap debridement v/s polytetrafluroethylene membrane in treatment of furcation lesions**.** ***Hom lay Wang etal 1994*** [84] also reported significant reduction in horizontal probing depth in sites treated with collagen membrane as barrier as compared to open flap debridement. Statistically significant attachment level gain is seen in both groups compared to the baseline and intergroup comparisons were not significant.

Both groups I and II showed statistically significant improvement in hard tissue parameters from baseline to 9 months post-surgery. Group I showed a defect fill of 1.20mm at 3 months and 1.84mm at 6 months and 2.2mm at 9 months compared to group II which showed 0.60mm at 3 months and 1.10mm at 6 months and 1.52mm at 9 months post operatively. Metformin group showed a statistically significant bone fill than open flap debridement with guided tissue regeneration alone. This substantiates the bone sparing and formative capacity of metformin, supported by ***Bak E J et al 2010***[62] study on effect of metformin on alveolar bone.

Metformin group showed a defect fill percentage of 39.20% at 3 months compared to 22.4 % in group II cases, 58.80 % at 6 months compared to 39.10% in

group II and 73% defect fill at 9 months compared to 56% of group II. This is similar to the reports by ***A.R .Pradeep etal*** [66, 67, 68]. With regard to radiographic parameters, metformin group showed a significant reduction in defect depth suggesting that metformin is effective in promoting bone formation.

SUMMARY AND CONCLUSION

The present study was conducted to evaluate bone regenerative potential of 1% Metformin gel in grade II furcation bony defect .In the present study 20 furcation defects categorized to study and control group were evaluated over a period of 3, 6, and 9 months.

In Group I the furcation areas were treated with 1% metformin gel and in group II debridement alone were done.

Following the cessation of a 9 month follow up, we found

1. An enhancement in clinical parameters like plaque index , gingival bleeding index, vertical and horizontal probing depth within study group.
2. An enhancement in clinical parameters like plaque index, gingival bleeding index, vertical and horizontal probing depth within control group.
3. Following radiographic evaluation of the study group at the end of 9 months, statistically significant defect fill was noticed.
4. The percentage of defect fill was 73±16.86 % at the end of 9months in the study group compared to 56.10±14.30 % in the control group.

From these constructive findings of our study we came to a conclusion that 1% metformin along with guided tissue regeneration using collagen membrane as barrier has superior bone regenerating capacity and can be used for reconstitution of periodontium lost by periodontal disease.

However, the limitations of this study are the smaller sample size which affected the statistical analysis of the results. Long-term analysis is also required to

determine the stability of the results. Further, well-controlled studies including larger sample size are needed to confirm the osteogenic potential of metformin for treating periodontal bony defects.

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Annexure 1

Participant information sheet English

Investigator: JENAPRIYA.R Guide: K. Malathi, MDS

Title: EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS -A RANDOMIZED CONTROLLED CLININCAL TRIAL.

Name of the research institution: Tamilnadu Government Dental College and Hospital, Chennai

The investigator, Dr. JENAPRIYA.R under the guidance of Dr. K MALATHI, MDS is conducting a study as titled above with aim to do an evaluation of efficacy of 1% metformin in the treatment of grade II furcation defects in chronic periodontitis .

1. **Procedure : the following examinations and investigations will be done for you.**
    - Intraoral examination, Extra oral examination
    - X-ray will be taken for the diseased site. Protection from radiographic x ray exposure will be given by thyroid collar, lead apron.
    - About 5ml (1 table spoon) of blood will be drawn from your hand for tests
    - Model of your teeth will be prepared by taking alginate impression
    - Deposits on your teeth will be removed with ultrasonic scaler and hand instrument.
    - Injection to anesthetise the surgical area will be given. Gum surgery will be done after attaining proper numbness. The gum tissue will be raised and the underlying bone defect will be cleaned and 1% metformin gel will be placed in to the defect.
    - Suitable medications will be given after surgery for pain and infection control
    - Clinical evaluation will be performed before surgical procedure, at 3 months, 6 months and 9 months after the procedure.
2. **Risk of participation:**
    - Patients may be allergic to LA or the material used in the study.
    - Patient may experience pain, discomfort, swelling following the procedure.

3 Human subject's protection

- Vulnerable population such as pregnant women, lactating woman and children will not be included in the study.
- Test dose will be given to check for allergy to LA.
- All instruments used in the study will be sterilized properly.
- Radiation protection measures will be taken while taking radiographs like thyroid collar, lead apron etc.

4. Benefits of participation:

Patients will be treated for improving the periodontal status and minimizing alveolar bone loss.

5. Confidentiality :

The identity of the patients participating in the research will be kept confidential throughout the study. In the event of any publication or presentation resulting from the research, no personally identifiable information will be shared.

6. Participants right :

Taking part in the study is voluntary. You are free to decide whether to participate in the study or to withdraw at any time; your decision will not result in any loss of benefits to which you are otherwise entitled. The results of this study will be intimated to you at the end of the study period or during the study if anything is found abnormal which may aid in the management or treatment.

7. Compensation: Nil

8. Contacts:

For queries related to the study:	**Contact details regarding rights of the participant:**
Primary Investigator: Dr.JENAPRIYA.R Contact Details: PG Student Department of Periodontics Tamilnadu Govt. Dental College & Hospital Chennai-600 003. Phone number:8939105508	Dr. B. Saravanan, MDS,PhD, The Chairperson, Institutional Ethical committee Tamilnadu Govt. Dental College & Hospital, Chennai-600 003.

பங்கேற்பதினால் வரக்கூடிய பக்க விளைவுகள்: வலி, வீக்கம் மற்றும் பயன்படுத்தும் பொருட்களினால் சில நேரங்களில் ஒவ்வாமை ஏற்பட வாய்ப்புண்டு. அதற்காக தேவைப்படும் மருந்துகளும் மருத்துவமும் வழங்கப்படும்.

பங்கேற்பதினால் விளையும் நன்மைகள்: உங்களின் நாள்பட்ட பல் ஈறு நோய்க்கு சிகிச்சை அளிக்கப்படும்.

இரகசிய காப்பு: உங்களைப் பற்றிய குறிப்புகள் பிறர் அறியா வண்ணம் ஆராய்ச்சி முடியும் வரை இரகசியமாக பாதுகாக்கப்படும். அதை வெளிப்படுத்தும் நேரங்களில் எந்த தனி அடையாளங்களும் வெளிப்பட வாய்ப்பு கிடையாது.

தன்னார்வ பங்கேற்பு: இந்த ஆராய்ச்சியில் பங்குபெறுவது தங்களின் தனிப்பட்ட முடிவு மற்றும் இந்த ஆராய்ச்சியில் இருந்து நீங்கள் எப்போது வேண்டுமானாலும் விலகிக்கொள்ளலாம். தங்களின் இந்த திடீர் முடிவு உங்களுக்கோ அல்லது ஆராய்ச்சியாளருக்கோ எந்தவித பாதிப்பும் ஏற்படுத்தாது என்பதை தெரியப்படுத்துகிறோம்.

நோயாளியின் பெயர் **கையொப்பம்/ கைரேகை**

ஆராய்ச்சி தொடர்புடைய தகவல்களுக்கு
மரு.ஜெனப்ரியா,
முதுநிலை மாணவர்,
பல்புறத்திசுவியல் துறை,
தமிழ்நாடு அரசு பல் மருத்துவக் கல்லூரி
மருத்துவமனை, சென்னை-3.
செல்: 8939105508

பங்கேற்பாளரின் உரிமை தொடர்புடைய தகவல்களுக்கு: மரு.பி.சரவணன்
தலைவர், நிறுவன நெறிமுறைகள் குழு,
தமிழ்நாடு அரசு பல் மருத்துவக் கல்லூரி
மற்றும் மருத்துவமனை, சென்னை-3.

ஆராய்ச்சி பற்றிய தகவல் படிவம்

ஆராய்ச்சி மேற்கொள்பவர்
மருத்துவர்.ஜெனப்ரியா

வழிநடத்துபவர்
மருத்துவர்.கே.மாலதி, எம்.டி.எஸ்

ஆராய்ச்சி நிறுவனத்தின் பெயர்: தமிழ்நாடு அரசு பல் மருத்துவக் கல்லூரி மற்றும் மருத்துவமனை, சென்னை.

ஆராயச்சியின் தலைப்பு

நாள்பட்ட பல் ஈறு நோயில் இரண்டாம் தர பல் வேர் பிரிவு பகுதி எலும்பு தேய்மானத்தில் 1% மேட்போர்மின் அரைதிண்மக் கரைசல் பயன்படுத்தி மதிப்பிடுதல்- ஒரு ஒப்பீட்டு மருத்துவ ஆய்வு.

ஆராய்ச்சியின் நோக்கம்

நாள்பட்ட பல் ஈறு நோயில் இரண்டாம் தர பல் வேர் பிரிவு பகுதி எலுவம்பு தேய்மானத்தில் 1% மேட்போர்மின் அரைதிண்மக் கரைசல் பயன்படுத்தி மருத்துவ மற்றும் கதிர் இயக்க மதிப்பீடு அறுவை சிகிச்சைக்கு முன் 3, 6 மற்றும் 9 மாத காலத்திற்கு மதிப்பீடு செய்தல். செயல்முறை கீழ்கண்ட ஆய்வுகள்/ பரிசோதனைகள் உங்களுக்காக செய்யப்படும்.

- வாய் பரிசோதனை
  - உட்புறம்
  - வெளிப்புறம்
- வழக்கமான இரத்தப் பரிசோதனை
- உங்களின் கைகளிலிருந்து இரத்தப் பரிசோதனைக்காக 5மி.லி. அளவு (ஒரு மேஜைக் கரண்டி அளவு) இரத்தம் எடுக்கப்படும்.
- நோயுற்ற பகுதியின் ஊடுகதிர் படம்
- சிகிச்சை தேவைப்படும் பல்லின் அளவானது அல்ஜினேட் அச்சு கொண்டு எடுக்கப்படும்.
- ஒவ்வாமை ஏற்படுகிறதா என்பதை தெரிந்துகொள்ள 0.5மி.லி 2% லிக்னோகெயின் மயக்க மருந்து உங்களின் கையில் பரிசோதனைக்காக செலுத்தப்படும். பின்பு நோயுற்ற பகுதியில் மயக்க மருந்து கொடுக்கப்படும்.

அல்ட்ரா சோனிக் ஸ்கேலர் மற்றும் கைக்கருவிகள் பயன்படுத்தி பல் மற்றும் பல்லின் வேர் சுத்தம் செய்யப்படும். உப்புநீர் கொண்டு நோயுற்ற பகுதி சுத்தம் செய்யப்படும்.

1% மேட்போர்மின் அரை திண்மக் கரைசல் பயன்படுத்தி நாள்பட்ட பல் ஈறு நோயில் இரண்டாம் தர பல்வேர் பிரிவு பகுதி எலும்பு தேய்மானத்தை மதிப்பிட்டு மருத்துவ மற்றும் கதிர் இயக்க மதிப்பீடு தொடர் நிலையில் 3, 6 மற்றும் 9 மாத காலத்திற்கு மதிப்பீடு செய்தல்.

Annexure :3

Informed Consent Form

"EVALUATION OF LOCALLY DELIVERED 1% METFORMIN GEL IN THE MANAGEMENT OF GRADE II FURCATION IN CHRONIC PERIODONTITIS -A RANDOMIZED CONTROLLED CLININCAL TRIAL."

Participant ID No:

"I have read the foregoing information, or it has been read to me. I have had the opportunity to ask questions about it and any questions I have asked have been answered to my satisfaction. I consent voluntarily to participate as a participant in this study and understand that I have the right to withdraw from the study at any time without in any way it affecting my further medical care."

_____	_____	_____
Date	Name of the participant	Signature/thumb impression
		Of the participant

[The literate witness selected by the participant must sign the informed consent form. The witness should not have any relationship with the research team; If the participant doesn't want to disclose his / her participation details to others, in view of respecting the wishes of the participant, he / she can be allowed to waive from the witness procedure (This is applicable to literate participant ONLY). This should be documented by the study staff by getting signature from the prospective participant]

"I have witnessed the accurate reading of the consent form to the potential participant and the individual has had opportunity to ask questions. I confirm that the individual has given consent freely"

Date	Name of the witness	Signature of the witness
Date	Name of the Interviewer	Signature of the interviewer

ஆராய்ச்சி ஒப்புதல் படிவம்

ஆராயச்சியின் தலைப்பு

நாள்பட்ட பல் ஈறு நோயில் இரண்டாம் தர பல் வேர் பிரிவு பகுதி எலும்பு தேய்மானத்தில் 1% மேட்போர்மின் அரைதிண்மக் கரைசல் பயன்படுத்தி மதிப்பிடுதல்- ஒரு ஒப்பீட்டு மருத்துவ ஆய்வு.

பெயர் புறநோயாளி எண்

வயது/ பால் ஆராய்ச்சி சேர்க்கை எண்

முகவரி

தொலைபேசி

நான் ..... வயது ..... என்னுடைய சுய நினைவுடனும் மற்றும் முழு சுதந்திரத்துடனும் இந்த மருத்துவ ஆராய்ச்சியில் என்னை சேர்த்துக்கொள்ள ஒப்புதல் அளிக்கிறேன்.

கீழ்காணப்படும் நிபந்தனைகளுக்கு நான் சம்மதிக்கிறேன்.

நான் இந்த ஆராய்ச்சியின் நோக்கம் மற்றம் செயல்முறைகள் பற்றி முழுமையாக தெரிவிக்கப்பட்டுள்ளேன்.

இந்த பரிசோதனைக்காக ஈறுகளில் அறுவை சிகிச்சை செய்ய வேண்டியுள்ளதாக அறிகிறேன்.

சிகிச்சையின் போது 1% மெட்பார்மின் உபயோகிக்க சம்மதிக்கிறேன்.

என் உடல் நலம் பாதிக்ப்பட்டாலோ அல்லது எதிர்பாராத வழக்கத்திற்கு மாறான நோய்குறிகள் தென்பட்டாலோ அதற்கு சிகிச்சை பெற்றுக்கொள்வதற்கும் முழு உரிமை உள்ளதாக அறிகிறேன்.

நான் ஏற்கனவே உட்கொண்ட மற்றும் உட்கொள்கின்ற மருந்துகளிந் விபரங்களை ஆராய்ச்சியாளரிடம் தெரிவித்துள்ளேன்.

என் மருத்துவ குறிப்பேடுகளை இந்த ஆராய்ச்சியில் பயன்படுத்திக்கொள்ள சம்மதிக்கிறேன். இந்த ஆராய்ச்சி மையமும் ஆராய்ச்சியாளரும் என்னுடைய விபரங்கள் அனைத்தையும் இரகசியமாக வைப்பதாக அறிகிறேன்.

.....	.....	.....
நேயாளியின் பெயர்	கையொப்பம்	தேதி
.....	.....	.....
ஆராய்ச்சியாளர் பெயர்	கையொப்பம்	தேதி

Annexure: 5

PROFORMA FOR TREATMENT GROUP

Date : OP No.: SL.No.

Name : Age : Sex:

Occupation : Income :

Address : Phone Number :

CHIEF COMPLAINTS AND DURATION:

HISTORY OF PRESENT ILLNESS:

PAST MEDICAL HISTORY:

PAST DENTAL HISTORY:

FAMILY HISTORY :

PERSONAL HISTORY :

a) Oral Hygiene Practices :

b) Habits :

c) Menstrual History :

d) Menopause :

e) H/o. Stress Factor :

GENERAL EXAMINATION

a) Extra-Oral Examination

b) Examination of Lymphnodes

INTRA-ORAL EXAMINATION WITH CLINICAL FINDINGS:

Buccal mucosa:

Vestibule:

Hard palate:

Soft palate:

Tonsils:

Tongue:

Floor of the mouth:

Teeth:

Decayed

Missed

Filled teeth

Gingiva:

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding Index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Probing depth and attachment loss in millimeter:

Maxillary:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Mandibular:

CAL																
PPD																
	18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
PPD																
CAL																

Investigations:

1. Biochemical / Haematological Investigation :

2. Others :

   Blood Pressure :

   Test Dose for L.A:

RADIOGRAPHIC EVALUATION

Intra-Oral Periapical Radiograph (IOPA)

PROVISIONAL DIAGNOSIS

PROGNOSIS

TREATMENT PLAN

FITNESS FOR TREATMENT

TREATMENT DONE

DATE : PROCEDURE : SIGNATURE :

MAINTENANCE PHASE

EVALUATION AFTER - 3 MONTH

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

MAINTENANCE PHASE

EVALUATION AFTER - 6 MONTH

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

MAINTENANCE PHASE

EVALUATION AFTER - 9 MONTH

Gingiva

Plaque index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

Bleeding index

18	17	16	15	14	13	12	11	21	22	23	24	25	26	27	28
48	47	46	45	44	43	42	41	31	32	33	34	35	36	37	38

S.NO	CALCULATIONS	BASELINE	9 MONTHS
1	Pocket probing depth (mm)		
2	Clinical attachment level (mm)		

S.NO	INDICES	BASELINE	3MONTHS	6MONTHS	9MONTHS
1	Plaque index (Sillness &Loe,1964)				
2	Gingival bleeding index(Ainamo & Bay 1975)				

FURCATION EXAMINATION:

Horizontal probing depth(mm)				
	36	37	46	47
Vertical probing depth (mm)				

FURCATION DEFECT DEPTH EVALUATION

Baseline	After 3 months	After 6 months	After 9 months

Signature of P.G student **Signature of the professor**